RED CELL DISTRIBUTION WIDTH AND RATIO OF RED CELL DISTRIBUTION WIDTH TO SERUM CALCIUM AS PREDICTORS OF OUTCOME OF ACUTE PANCREATITIS

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BY

DR. SAVJOT SINGH NARANG

SUPERVISOR

DR. CHIRANJIV SINGH GILL

DEPARTMENT OF GENERAL SURGERY
DAYANAND MEDICAL COLLEGE AND HOSPITAL
LUDHIANA
(MAY,2021)

DECLARATION

I declare that the thesis entitled "**RED CELL DISTRIBUTION WIDTH AND RATIO OF RED CELL DISTRIBUTION WIDTH TO SERUM CALCIUM AS PREDICTORS OF OUTCOME OF ACUTE PANCREATITIS**" has been prepared by me under the guidance of **Dr. Chiranjiv Singh Gill**, Professor, Department of General Surgery, Dayanand Medical College and Hospital, Ludhiana. No part of this thesis has formed the basis for the award of any degree previously.

_____

Dr. Savjot Singh Narang
Department of General Surgery
Dayanand Medical College & Hospital
Tagore Nagar
Ludhiana-141001
Punjab.

Date:

CERTIFICATE

I certify that **Dr. Savjot Singh Narang** has prepared his thesis entitled "**RED CELL DISTRIBUTION WIDTH AND RATIO OF RED CELL DISTRIBUTION WIDTH TO SERUM CALCIUM AS PREDICTORS OF OUTCOME OF ACUTE PANCREATITIS**" for the award of the degree of M.S. in General Surgery of Baba Farid University of Health Sciences, under my guidance. He has carried out the work at the Department of General Surgery, Dayanand Medical College & Hospital, Ludhiana.

The data collected in this thesis is genuine and the work has been carried out by the candidate himself.

Supervisor

Dr. Chiranjiv Singh Gill
Professor
Department of Surgery
DMC&H, Ludhiana

Co- supervisors

Dr. Pavneet Kaur Selhi
Professor
Department of Pathology
DMC&H, Ludhiana

Dr. Varun Gupta
Associate Professor
Department of Surgery
DMC&H, Ludhiana

Date:

ENDORSEMENT BY THE HEAD OF THE DEPARTMENT AND PRINCIPAL

This is to certify that the thesis entitled "**RED CELL DISTRIBUTION WIDTH AND RATIO OF RED CELL DISTRIBUTION WIDTH TO SERUM CALCIUM AS PREDICTORS OF OUTCOME OF ACUTE PANCREATITIS**" is a bonafide research work done by **Dr. Savjot Singh Narang** under the guidance of **Dr. Chiranjiv Singh Gill**, Professor, Department of General Surgery, Dayanand Medical College & Hospital, Ludhiana.

Head of Department

Dr. Jaspal Singh
Professor & Head
Department of General Surgery
DMCH, Ludhiana

Principal

Dr. Sandeep Puri
Principal & Professor
Department of Medicine
DMCH, Ludhiana

Date:

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Dr. Savjot Singh Narang
Department of General Surgery
Dayanand Medical College & Hospital
Tagore Nagar
Ludhiana-141001
Punjab.

Date:

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Dedicated

to

my Family

&

Teachers

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DR. Savjot Singh Narang

ABBREVIATIONS

AP -	Acute Pancreatitis
MM -	Modified Marshall Score
ICU -	Intensive Care Unit
CRP -	C - Reactive Protein
BUN -	Blood Urea Nitrogen
BISAP -	Bedside Index for Severity in Acute Pancreatitis
SIRS -	Systemic Inflammatory Response Syndrome
RDW -	Red cell Distribution Width
RBC -	Red Blood Cells
TSC -	Total Serum Calcium
RDW:TSC -	Ratio of Red Cell Distribution Width to Total Serum Calcium
CCK -	Cholecystokinin
CARS -	Compensatory Anti-inflammatory Response Syndrome
AC -	Atlanta Classification
RAC -	Revised Atlanta Classification
CECT -	Contrast-enhanced Computed Tomography
MRI -	Magnetic Resonance Imaging
IEP -	Interstitial Edematous Pancreatitis
APFC -	Acute Peripancreatic Fluid Collection
ANC -	Acute Necrotic Collection
WON -	Walled-off Necrosis
ERCP -	Endoscopic retrograde cholangiopancreatography

APACHE - Acute Physiology and Chronic Health Evaluation

MRCS - Medical Research Council Sepsis

SAPS - Simplified Acute Physiology Score

LDH - Lactate Dehydrogenase

PCV - Packed Cell Volume

CTSI - Computed Tomography Severity Index

Hct - Hematocrit

TAP - Trypsinogen Activation Peptide

PMN - Polymorphonuclear

TNF - Tumor Necrosis Factor

IL - Interleukin

ARDS - Acute Respiratory Distress Syndrome

EN - Enteral Nutrition

PN - Parenteral Nutrition

RCT - Randomised Controlled Trials

NG - Nasogastric

TLC - Total Leucocyte Count

Sr No. - Serial Number

NJ - Nasojejunal

PaO2 - Partial pressure of oxygen

FiO2 - Fraction of inspired oxygen

USG - Ultrasonography

FNA - Fine Needle Aspiration

AUROC - Area Under Receiver Operating Characteristic curve

DOR - Discharge On Request

ABSTRACT

Introduction: Acute pancreatitis (AP) is the inflammation of pancreas induced by activation of the pancreatic enzymesdue to a variety of causes, of which gall stones and alcohol are the most common. Current severity scores include multiple variables, the results of which are available only after 48 hours of admission. Red cell distribution width (RDW) and total serum calcium (TSC) are simple routine parameters that seem to be related to inflammatory status and results of which are readily available.

Aims of Study: To evaluate RDW and RDW:TSC within 24-hours of admission as predictors of outcome (severity and mortality) and in-hospital intervention (medical/percutaneous drainage/surgical) required by patient of AP.

Material & Methods: Values of RDW and TSC along with data regarding treatment given was collected in this prospective randomized study of AP patients who were admitted in DMCH, Ludhiana over a period of 1 year spanning from 1 Jan, 2019 to 31 Dec, 2019. Diagnosis and severity was defined according the Revised Atlanta Classification 2012.

Results: Cut-off value for RDW (AUROC:0.997; p=0.000) to predict severity of AP was 16.25% (senstivity-100%; specificity-97.1%) while that of RDW:TSC (AUROC:1; p-0.000) was 2.42 (senstivity-100%; specificity-100%). Similarly, cut-off for RDW (AUROC:0.947; p=0.000) to predict mortality in AP was 17.20%(senstivity-100%; specificity-87.4%) and that of RDW-to-TSC ratio (AUROC:0.975; p-0.000) was 2.9 (senstivity-100%; specificity-96.6%). Both, RDW and RDW:TSC, were observed to be major predictors of severity and mortality in AP. Mean RDW for patients requiring endoscopicnasocystic drainage, necrosectomy, and percutaneous drainage of peripancreatic collection was 14.20 %, 17.38±0.685%, and 17.59±2.335% respectively while RDW:TSC requiring nasocystic drainage, necrosectomy and percutaneous drainage of peripancreatic collection were 2.21, 2.83±0.201 and 2.56±0.384 respectively.

Conclusion: Our study found that RDW and RDW:TSC were good prognostic predictors of severity and mortality in AP patients. These results indicate that RDW and RDW:TSC are convenient, economic, and sensitive monitoring methods for predicting severity and mortality in AP patients.

Keywords: Acute pancreatitis, Red cell distribution width, total serum calcium, severity, mortality.

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INTRODUCTION

Acute pancreatitis (AP) is characterized by the destruction and inflammation of pancreatic tissue due to activation of pancreatic acinar cells as a result of being triggered by various factors. AP can cause significant morbidity and mortality.[1] AP is one of the most common surgical diseases which can cause severe acute abdomen. Most cases (80–90%) are mild and self-limiting with a good outcome. The remaining 10–20% of patients with severe disease have either pancreatic necrosis or distant organ failure and usually require intensive care and possible operative intervention with a mortality rate of up to 40%.[2]

A clinically based classification system for acute pancreatitis, The Atlanta severity classification system, was established in the International Symposium on Acute Pancreatitis in Atlanta, Georgia, in 1992. The Atlanta severity classification system had certain flaws such as it was retrospective, the duration of organ failure was unspecified and local complications did not seem to increase mortality. The Atlanta classification was revised via an international, web-based consensus in 2012 to provide clear definitions for the classification of acute pancreatitis using easily identifiable clinical and radiological criteria. Greater emphasis was laid on organ failure using the Modified Marshall (MM) score and severity was graded as mild, moderately severe, and severe acute pancreatitis.[3]

Early diagnosis and precise staging of disease severity are important goals for the initial evaluation and management of acute pancreatitis. While patients with mild acute pancreatitis are usually managed with fluid resuscitation and supportive care, those with severe acute pancreatitis require an intensive care unit (ICU) with medical/endoscopic modalities readily available. Due to the risk of rapid deterioration in severe acute pancreatitis, the assessment of severity becomes crucial to a clinician.[4]

Early identification of AP patients with a high risk of mortality and appropriate evaluation of the severity of AP is important for early medical treatment of AP to reduce the mortality rate of severe AP. An

ideal marker/prognostic score should be simple, economic, noninvasive, accurate, and quantitative.[5]

In previous studies, several AP scoring systems and laboratory tests have been proposed to estimate the prognosis of AP, such as Ranson's score, Balthazar score, BISAP score and SIRS score, C-reactive protein (CRP), serum blood urea nitrogen (BUN), D-dimer and pro-calcitonin levels.[5] Ranson and Bedside Index for Severity in AP (BISAP) are specific and widely used prognostic scoring systems due to easy evaluation and availability in the first 24 h.[6]

C-reactive protein (CRP) was found to be a useful single serum marker to predict the severity of AP.[7] But CRP ≥15 mg/dL was found to be a predictor of poor prognosis only at 48hrs, and therefore a limited severity discriminator in the early phase of AP.[6,7]

There are multiple disadvantages associated with score systems such as the hassle of calculation and the need for ordering specific tests.[7] Until now, no single serum marker can predict severity or mortality in AP at admission.

Red cell distribution width (RDW) is a routine parameter of the complete blood count test. RDW is a simple, easy, inexpensive, and quantitative test that measures the size heterogeneity of peripheral red blood cells (RBC), known as anisocytosis. RDW has also been associated with inflammatory markers such as CRP, interleukin-6, and fibrinogen. It is a commonly performed test in almost all the patients at the time of admission.[8] Conventionally, RDW has been instrumental to explore the etiologies of anemia.[8] During the past decade, however, many studies have shown the role of RDW in assessing the risk, disease activity, and prognosis of various diseases, such as malignancies[9], heart failure[10], autoimmune diseases[11], and hepatocellular carcinoma[12], etc. RDW was also found to be a good predictor of mortality risk in the elderly, critically-ill patients, and patients with acute or chronic cardiovascular and respiratory diseases.[13] Besides those conditions, RDW has also been evaluated as a mortality predictor in AP.[14-16]

Hypocalcemia has been associated with AP severity but its etio-pathogenesis has been debated for decades. Centuries-old

literature reported that in 1890, Langerhans observed calcium deposits in areas of fat necrosis. Later in 1944, Edmondson reported that hypocalcemia was due to the formation of calcium soaps.[17] In 1975, Condon et al. reported a decrease in parathyroid hormone levels in patients with hypocalcemia and normocalcemia and postulated that parathyroid hormone depletion was the main induction factor of persistent hypocalcemia in AP.[17] In 1976, Imrie et al. associated hypocalcemia with hypoalbuminemia and proposed that total serum calcium (TSC) should be corrected considering albumin concentration before taking therapeutic measures.[18] AP studies using animal experimental models have observed a decrease in ionized calcium and total calcium concentrations after 6 to 18 hours of pancreatitis induction, in addition to the fact that the onset of hypocalcemia is associated with the accumulation of calcium in the soft tissues.[19,20] More recently, the role of the parathyroid hormone has been again reviewed in relation to the pathogenesis of hypocalcemia in AP, and it has been reported that the condition is the result of an inadequate parathyroid response; it is even probable that, just as in other critical diseases, its origin is multifactorial.[21-24] Given its importance, TSC has a place in some of the AP prognostic severity scales.[25] Individually, it has been evaluated as an important mortality prognostic factor [26,27] and it has also been evaluated as a predictor of severe AP.[28]

In our study, we will use RDW and ratio of RDW to total serum calcium (TSC) values to predict outcome and in-hospital intervention required by patient of AP. This will decrease the burden of unnecessary expensive tests and scores which require complicated calculations. This will also allow to timely plan for interventions which in return would help to decrease morbidity and mortality of the patients.

AIMS AND OBJECTIVES

In AP, to evaluate red cell distribution width and ratio of red cell distribution width to serum calcium within 24hours of admission as predictors of

- outcome (severity and mortality)
- in-hospital intervention (medical/ percutaneous drainage/surgical) required

REVIEW OF LITERATURE

History of Pancreas

Herophilus, a Greek anatomist and surgeon, apparently first discovered the pancreas.[29] Four hundred years after Herophilus, Ruphos in the 1st or 2nd Century AD, an anatomist and surgeon of Ephesus, gave the name — pancreas derived from Greek, 'pan (all) and kreas(flesh)'.[30] Galen (Claudius Galenus 138-201 AD), "Physician to the Gladiators" of Rome & the Roman Emperor, proposed that the pancreas serves as a cushion to protect the large blood vessels lying behind it.[31]

The pancreatic duct was discovered on March 2nd, 1642 by a German émigré, Johann Georg Wirsüng[32], in the San Francisco Monastery in Padua, Italy. The enlargement of the main pancreatic duct of Wirsung at its junction with the common bile duct and its projection into the duodenum was described as Papilla by Vater in 1720. The accessory duct of Santorini was so named after its discoverer, fourteen years after the discovery of the main pancreatic duct.

In 1893, Laguesse suggested that the islet cells produce a hormone. In 1909, the name 'insulin' for this hormone was suggested by Jean de Meyer. Eugene Lindsay Opie (1873-1971) was able to show the association between diabetes and failure of the islet cells and in 1901, proposed his "common channel "hypothesis.[33]

In 1652, Nicolaes Tulp (1593-1674), a Dutch physician and anatomist, published the first clear description of acute pancreatitis. Reginald Huber Fitz (1843-1913), an American pathologist and professor at Harvard Medical School, presented the first systematic analysis of acute pancreatitis, in 1889, with its various types and described them as pancreatic hemorrhage, suppurative and gangrenous pancreatitis, and disseminated fat-necrosis.[34] Based on Fitz's systematic clinical and bedside observations,he proposed an operation in the early stages of this disease as extremely hazardous.[31] However, Fitz subsequently abandoned this conservative stance, and in 1903, he proposed surgery in cases of acute pancreatitis as the most satisfactory method of treatment, and, like most abdominal operations for the relief of acute

symptoms, is more helpful the earlier in the course of the disease it is performed.

During the 20th century, different theories have been proposed concerning whether surgery or conservative treatment is to be preferred. In the 1930s, there was a change to a more conservative approach due to high mortality rates observed after surgical interventions. During the 1960s and 1970s, surgery became more popular, including blunt necrosectomy for necrotizing pancreatitis. Fitz was mistaken concerning the underlying pathophysiological cause of acute pancreatitis.

In 1896, Hans Chiari (1851-1916), Professor of pathology in Prague, postulated that pancreatic autodigestion was the mechanism of the disease, meaning that the pancreas —succumbs to its digestive properties.

Claude Bernard (1813- 1878), the French physiologist, demonstrated the role of pancreatic secretions in the digestion of proteins, carbohydrates, and fats. Bernard concluded the presence of fat in stoolsas pathognomonic for the failure of pancreatic juice to reach the intestine. This was the starting shot for pancreatic exocrine replacement therapy.

Even if the history of research concerning acute pancreatitis and its complications is long and successful, many issues still remain to be discovered and developed.

Embryology

At the 4th week of gestation, the pancreas develop from two endodermal buds that originate from the duodenum.The outpouchings are the dorsal pancreatic bud and ventral pancreatic bud. The dorsal pancreas outgrows the ventral pancreas and the ventral pancreas rotates toward the dorsal pancreas as it is carried by the common bile duct. Finally, on the 37th day of intrauterine life, both dorsal and ventral pancreatic buds and the ductal systems fuse so that secretions from the ventral pancreas enter the shared ductal system of the ventral pancreas and common bile duct. Most of the head, body, and tail of the pancreas

develop from the dorsal bud. Uncinate process and inferior part of the head of pancreas develop from the ventral bud.[35,36]

Anatomy [37-39]

The pancreas is an elongated, non-capsulated, multi-lobular gland that extends transversely from the second part of the duodenum to the splenic hilum across the posterior abdominal wall. It corresponds to the level of the first or second lumbar vertebra. It is a J-shaped gland lying posterior to the stomach and separated from it by lesser sac. It is about 15-18 cm in length, 1-4cm broad, and 1-3cm in thickness. The weight of pancreas is about 80 to 100gms. Anatomically, it is divided into head, neck, body, and tail. The head lies to the right of midline within the duodenal C loop, immediately anterior to the vena cava at the confluence of the renal veins. The uncinate process extends from the head of the pancreas behind the superior mesenteric vein and terminates adjacent to the superior mesenteric artery. The neck of the gland extends medially from the head to lie anterior to those vessels. The body extends laterally from the neck towards the spleen, whereas the tail extends into the splenic hilum

The main pancreatic duct of Wirsung begins at the tail and passes along the body of pancreas. In the head region of pancreas, it joins with CBD to form hepatopancreatic ampulla of Vater which opens at the major duodenal papilla in the second part of duodenum.

The accessory pancreatic duct of Santorini begins in the lower portion of the head, crosses in front of the main duct with which it communicates, and opens into the minor duodenal papilla.

Arterial supply [37,38]

The pancreas is supplied by a complex arterial network arising from the celiac trunk and superior mesenteric artery. The head and uncinate process are supplied by pancreaticoduodenal arteries (anterior and posterior), which arises from the hepatic artery via the gastroduodenal artery superiorly, and superior mesenteric artery inferiorly. The neck body and tail receive arterial supply from the splenic artery.

Venous drainage [37,38]

Its venous drainage is through tributaries of the splenic vein, superior mesenteric vein, and then into portal veins.

Lymphatic drainage [37-39]

They drain into pancreaticosplenic, coeliac, and superior mesenteric groups of lymph nodes.

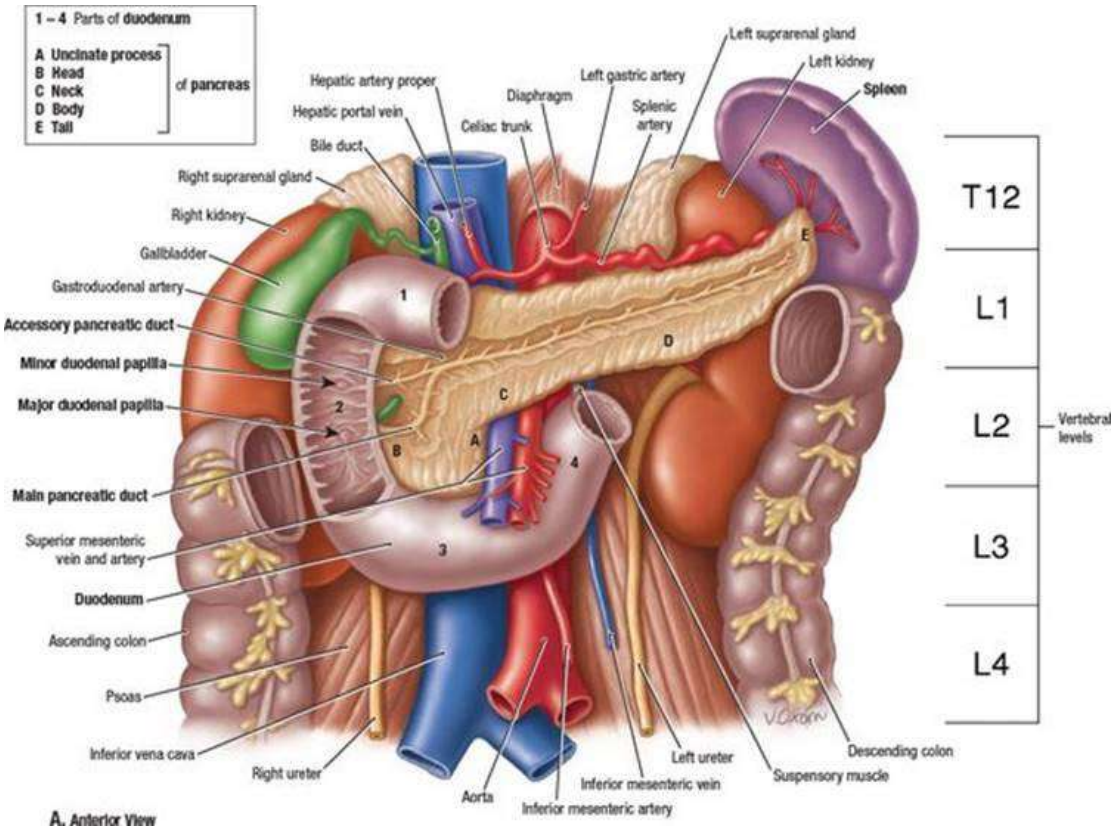

Fig.1 Anatomy of Pancreas [40]

Physiology of Pancreas [41]

The pancreas is a mixed gland that has both exocrine and endocrine secretions. Exocrine secretion has two components, enzyme secretion which originates from the acinar cells, and electrolyte secretion which originates from the centriacinar and intercalated duct cells. Approximately 2.5 L (0.2 to 0.3 ml/min) of clear, colorless, bicarbonate-rich pancreatic juice is secreted by the human pancreas each day, containing 6 to 20 grams of proteins. It plays a critical role in food digestion and alkalization of the duodenum.

Enzyme secretion

The enzymes present in pancreatic juice have a major role in digestion. Pancreatic secretions are controlled in part by a reflex mechanism and in part by gastrointestinal hormones, secretin, and CCK (Cholecystokinin).[42] Powerful protein splitting enzymes of the pancreatic juice are secreted in form of inactive pro-enzymes. As the pancreatic juice enters the duodenum, trypsinogen is converted to the active enzyme trypsin by the brush border enzyme enteropeptidase (enterokinase). Trypsin then converts chymotrypsinogen into chymotrypsin and other pro-enzymes into active ones. Trypsin can also activate trypsinogen, therefore once some trypsin is formed, there occurs an autocatalytic chain reaction.

There is always potential danger of the release of a small amount of trypsin into the pancreas thus resulting in a chain reaction that would produce active enzymes causing auto-digestion of the pancreas. It is therefore not surprising that the pancreas normally contains a trypsin inhibitor.[42]

Another enzyme activated by trypsin is phospholipase A2 which splits a fatty acid, lecithin, forming lysolecithin which damages cell membranes. It has been hypothesized that in acute pancreatitis phospholipase A2 is activated in pancreatic ducts, thus forming lysolecithin from the lecithin which is a normal constituent of bile. This disrupts pancreatic tissue and causes necrosis of surrounding fat.[42]

Pancreatic exocrine secretion is also influenced by inhibitory neuropeptides which include somatostatin, pancreatic polypeptide, peptide YY, neuropeptide Y, enkephalin, pancreastatin, calcitonin gene-related peptides, glucagon & galanin. Although pancreatic polypeptide and peptide YY primarily act on nerves outside the pancreas, somatostatin acts at multiple sites. A small amount of pancreatic digestive enzymes normally leak into the circulation, but in acute pancreatitis, the circulating levels of the digestive enzymes rise markedly thus making plasma concentration of amylase or lipase concentration a valuable marker in diagnosing the disease.

Auto digestion of the pancreas is prevented by

1. Pancreatic proteases stored as pro-enzyme

2. Intracellular calcium homeostasis (destruction of spontaneously activated trypsin if low intracellular calcium is present in the cytosol of the acinar cell)

3. acid-base balance

4. The synthesis of protective protease inhibitors (20% of intracellular trypsin activity is inhibited by pancreatic secretory trypsin inhibitor [PSTI] or SPINK1) Chymotrypsin C can also lyse and inactivate trypsin. These protease inhibitors are found in the acinar cell, the pancreatic secretions and the α1and α2globulin fractions of plasma.

If any of these four protective mechanisms is lost, it can leads to premature enzyme activation, autodigestion, and acute pancreatitis.

Acute Pancreatitis

According to the Atlanta Symposium[43], acute pancreatitis was defined as an acute inflammatory process of the pancreas that may also involve peri-pancreatic tissues and/or remote organ systems.

Etiology of Acute Pancreatitis [38,43-49]

Determining the etiology of AP is crucial in the management of an acute episode and the prevention of recurrent pancreatitis. Relative frequency depends on the patient population and prevalence of alcoholism in the population studied. In the United States, alcohol abuse is the main cause while in Europe and Asia, gall stone associated pancreatitis predominates. Also, females are more prone to gall stone pancreatitis and males for alcohol-induced pancreatitis.[44]

Common causes of acute pancreatitis are

i. Alcohol.

ii. Choledocholithiasis / gall stones.

iii. Hyper triglyceridemia.

iv. Trauma.

v. ERCP.

vi. Post-operative.

vii. Drugs (Azathioprine, Mercaptopurine, Valproic acid, Estrogens, Tetracycline, Metronidazole, Nitrofurantoin, Furosemide, Sulfonamide,

Methyldopa, Cimetidine, Ranitidine, Didanosine, Acetaminophen, erythromycin.).

viii. Sphincter of Oddi dysfunction.

xi. Toxins (Ethyl alcohol, Methyl alcohol, scorpion venom, organophosphorus, insecticides)

Uncommon causes of acute pancreatitis are

i. Vascular causes and vasculitis.

ii. Connective tissue disorders.

iii. Carcinoma pancreas.

iv. Hypercalcemia.

v. Periampullary diverticulum.

vi. Pancreas divisum.

vii. Hereditary pancreatitis.

viii. Cystic fibrosis.

xi. Infections (Parasitic- Ascariasis, Clonorchiasis. Viral - Mumps, Rubella, Hepatitis A, B, non-A, non-B, Coxsackie Virus-B, Echovirus, adenovirus, cytomegalovirus, varicella, Epstein bar virus, Human Immunodeficiency virus. Bacterial- Mycoplasma, Campylobacter jejuni. Mycobacterium tuberculosis, Mycobacterium avium complex, Legionella, Leptospirosis)

Table 1. Etiology of pancreatitis.[50,51] **Conditions that are associated with an increase in the likelihood of developing acute pancreatitis.**

Etiology	**Salient Features**
Cholelithiasis	Gallstone obstruction of ampulla results in reflux of bile. Edema during the passage of stone is another potential inciting event. Variable incidence (35-60%)
Alcohol	Second most common cause. Alcohol lowers the threshold for trypsin activation and sensitizes the pancreas to injury via various mechanisms such as calcium signaling, zymogen secretion, unfolded protein response,

	and by altering mitochondrial membrane integrity.
Smoking	Independent dose-dependent risk factor. Synergistic effect with alcohol.
Post ERCP	Due to mechanical trauma to the papilla leading to obstruction to the outflow of pancreatic juice and administration of radiological contrast media.
Hypertriglyceridemia	Most commonly found in association with gestational pancreatitis.
Hypercalcemia	Very rare. Usually a diagnosis of exclusion.
Autoimmune	Steroid responsive and commonly associated with chronic pancreatitis.
Hereditary	Autosomal dominant with 80% penetrance. Mutation of Serine protease 1 gene (PRSS1) on chromosome 7q35 which encodes trypsinogen.
Miscellaneous	Hemorrhagic shock, Systemic lupus erythematosus, Penetrating peptic ulcer, Crohn's disease, Reye's syndrome, Polyarteritis nodosa, Thromboembolism, Pregnancy

Pathogenesis of Acute Pancreatitis

The pathogenesis of acute pancreatitis is only known partially. Two possible main mechanisms for initiating gallstone and alcoholic pancreatitis are duct obstruction and acinar cell injury. The passage of gallstones through the common bile duct can cause transient obstruction of the pancreatic duct. This obstruction of the pancreatic duct increases the hydrostatic pressure within the pancreatic duct, leading to blockage of pancreatic secretion and subsequent activation of pancreatic enzymes within the pancreas.[52] In alcoholic pancreatitis, it is postulated that ethanol and its metabolites cause oxidative stress

leading to toxic effects on the pancreatic acinar cells which predisposes the gland to autodigestive injury.[52]

There is still so much left to learn about pathophysiological mechanisms explaining the activation and release of pancreatic enzymes, and the progression from an initially localized disease to a systemic inflammatory response and potential multiple organ failure. Most investigators agree that premature activation of the pancreatic pro-enzyme trypsinogen to the active enzyme trypsin within the pancreas is the central event in the pathogenesis of acute pancreatitis.[53]

There are only three known ways of activation of trypsinogen: by enterokinase, cathepsin B, and auto-activation. Trypsin activates other pancreatic pro-enzymes and pro-inflammatory cascade systems (including the complement system, the kinin system, the coagulation system, the fibrinolytic system, and macrophages). Premature enzymatic activation leads to autodigestion of pancreatic tissue which is histologically characterized by acinar cell necrosis and parenchymal inflammatory infiltrates.

In the severe form of pancreatitis, the local injury further leads to a generalized hyper inflammation, SIRS (Systemic Inflammatory Response Syndrome), associated with the potential failure of distant organs. SIRS [54,55] is identified by the presence of two or more of the following criteria:

- Temperature > 38° Celsius or < 36° Celsius
- Respiration >20 beats/min
- Pulse >90 beats/min
- White blood cell count > 12,000 cells/mm^3 or < 4000 cells/mm^3 or more than 10% immature forms.

Detecting the presence of SIRS gives critical prognostic data. 25-60% of patients present with SIRS on admission[56,57], but this usually resolves within 24 hours of admission for more than 50% of these patients upon adequate fluid resuscitation.[56] A persistent SIRS within the first 24 hours following admission and fluid resuscitation increases

the risk of persistent organ failure and necrosis, thereby increasing the risk of death.[57]

The hypoinflammatory state i.e. the compensatory anti-inflammatory response syndrome (CARS) may follow during critical illness.[55] These patients are more vulnerable to an infection either by bacterial translocation or the trauma added by surgical intervention during CARS. This could further lead to sepsis.[58,59]

However, It still remains unclear why some cases progress to the necrotizing form of acute pancreatitis and develop multiple organ failure, whereas others suffer only from milder forms.

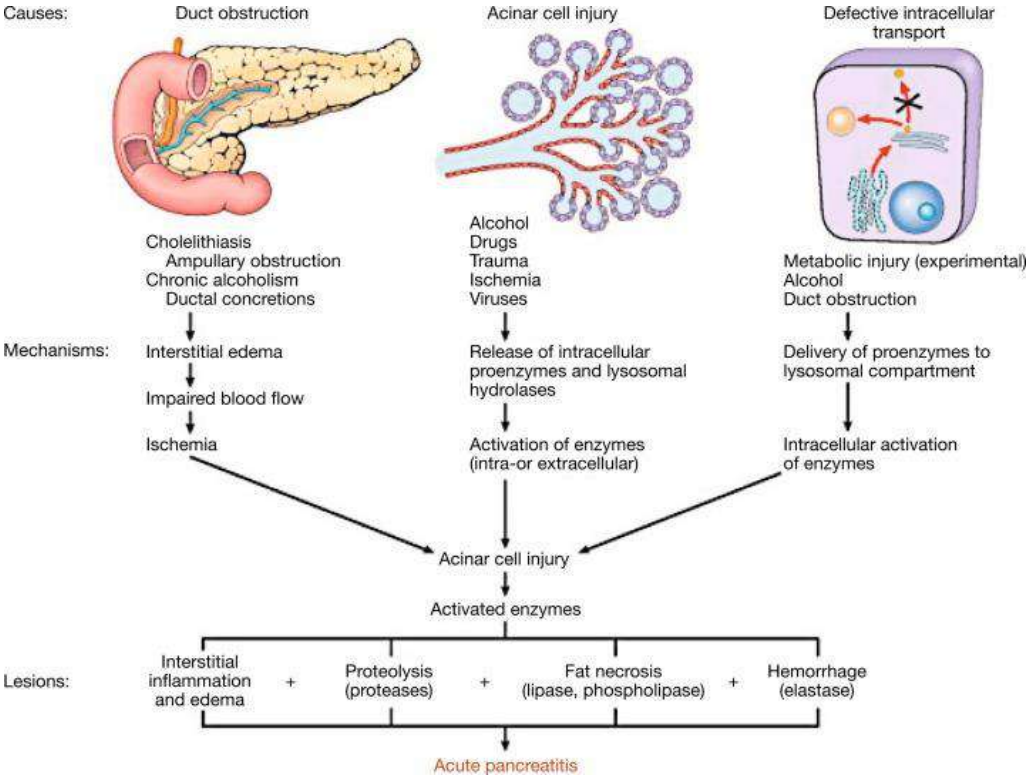

Fig 2. Etiopathogenesis of Acute Pancreatitis [60]

Clinical Presentation of Acute Pancreatitis

A reasonably secure diagnosis is often possible based solely on clinical presentation. In more than 90% of patients, the predominant feature is pain abdomen. Pain is mostly in the epigastrium, constant, boring, or penetrating, and may radiate to the back. The pain usually starts 12 to 48 hours after taking alcohol or after a large meal in case of gallstone pancreatitis.

Other features include fever, vomiting, tachycardia, epigastric tenderness, hypoactive and absence of bowel sounds, and abdominal distension. Sometimes a mass can be palpable in the epigastrium. In about 3% of patients, bluish discoloration in the left flank (Grey Turner's sign) or around the umbilicus (Cullen's sign) may be appreciated in pancreatitis. These signs are due to tracking of blood-stained retroperitoneal fluid along the planes of the abdominal wall to the flank or along the falciform ligament to the umbilical area and indicate a severe episode of acute pancreatitis.[61]

Jaundice can also be seen in patients with distal common bile duct obstruction by a gallstone or compression by pancreatic edema. In severe acute pancreatitis, hypovolemia, hypotension, hypoperfusion, and obtundation may be present.

Other manifestations include pleural effusion (mostly left side), ascites, and elevation of left hemi-diaphragm with tachypnoea, dyspnoea, and cyanosis. Less commonly, subcutaneous fat necrosis and disseminated intravascular coagulation can be seen.

Atlanta Classification System

In 1992, the international symposium in Atlantaestablished a worldwide adopted system to reach a global consensus on terms and descriptions of AP. The Atlanta classification (AC) was a clinically-based framework proposed by 40 internationally recognized experts containing descriptive terms of local and systemic complications as well as a disease stratification into mild and severe. However, after 20 years of assessment, considerable inconsistencies regarding the application of nomenclature and interpretation of terminology of the AC have been demonstrated.[62-67] Additionally, substantial progress has been made in the understanding of pathophysiological pathways, disease-related complications, and morbidity as well as imaging and surgical interventions. Thus, in 2012 the revised Atlanta classification of 2012 (RAC) was introduced for assessment of AP severity. In this classification, several definitions are stated including diagnosis of AP, detailed morphological features, and contrast-enhanced computed tomography (CECT) criteria of local complications (table 2). The

symposium also discarded terms like phlegmon, infected pseudocyst, and hemorrhagic pancreatitis. The RAC defines systemic complications as deterioration of co-morbidities and organ failure according to the modified Marshall scoring system (table 3).[3,58]

As per RAC[3,43], the diagnosis of acute pancreatitis requires two of the following three features:

a) Abdominal pain consistent with acute pancreatitis (acute onset of persistent, severe, epigastric pain often radiating to the back).

b) Serum lipase activity (or amylase activity) at least three times greater than the upper limit of normal.

c) Characteristic findings of acute pancreatitis on contrast-enhanced computed tomography (CECT) and less commonly magnetic resonance imaging (MRI) or Trans-abdominal ultrasonography.

The onset of acute pancreatitis is defined as the time of onset of abdominal pain (not the time of admission to the hospital).

Table 2 Morphological features and CECT criteria in AP according to the RAC

Morphology groups	CECT Criteria	Time
Interstitial edematous pancreatitis (IEP)	Homogenous enhancement of the pancreatic parenchyma, normal or minor inflammatory changes of the peri-pancreatic tissue (see below - APFC or pancreatic pseudocyst)	-
Necrotising Pancreatitis	Heterogeneous enhancement of the pancreatic parenchyma and/or peri-pancreatic tissue necrosis (see below – ANC or WON)	-
Acute Peripancreatic Fluid Collection (APFC)	Homogeneous fluid density. No complete wall. No necrosis. Associated with IEP. Solely extra-pancreatic location.	≤ 4 weeks

Pancreatic Pseudocyst	Homogeneous fluid density. Fully encapsulated. No necrosis. Associated with IEP. Solely extra-pancreatic location.	> 4 weeks
Acute necrotic collection (ANC)	Heterogeneous and non-liquid density. No complete wall. Associated with necrotizing pancreatitis. Intra- or extra-pancreatic location	≤ 4 weeks
Walled-off necrosis (WON)	Heterogeneous and non-liquid density. Fully encapsulated. Associated with necrotizing pancreatitis. Intra- or extra-pancreatic location	> 4 weeks

Table 3. Modified Marshall scoring system for organ failure - A score of 2 or more equals organ failure

	Score				
Organ system	**0**	**1**	**2**	**3**	**4**
Respiratory (PaO_2/FiO_2)	>400	301–400	201–300	101–200	≤101
Renal*					
(serum creatinine, μmol/l)	≤134	134–169	170–310	311–439	>439
(serum creatinine, mg/dl)	<1.4	1.4–1.8	1.9–3.6	3.6–4.9	>4.9
Cardiovascular (systolic blood pressure, mm Hg)†	>90	<90, fluid responsive	<90, not fluid responsive	<90, pH<7.3	<90, pH<7.2

For non-ventilated patients, the FiO_2 can be estimated from below:

Supplemental oxygen (l/min)	**FiO_2 (%)**
Room air	21
2	25
4	30
6–8	40
9–10	50

A score of 2 or more in any system defines the presence of organ failure.
*A score for patients with pre-existing chronic renal failure depends on the extent of further deterioration of baseline renal function. No formal correction exists for a baseline serum creatinine ≥134 μmol/l or ≥1.4 mg/dl.
†Off inotropic support.

This classification also defines three degrees of severity: mild acute, moderately severe acute, and severe acute pancreatitis. Transient organ failure is present for <48 hours whereas persistent organ failure is defined as organ failure that persists for >48 hours.

a) Mild acute pancreatitis - Mild acute pancreatitis is characterized by the absence of organ failure and the absence of local or systemic complications.

b) Moderately severe acute pancreatitis - Moderately severe acute pancreatitis is characterized by the presence of transient organ failure or local or systemic complications in the absence of persistent organ failure.

c) Severe acute pancreatitis - Severe acute pancreatitis is characterized by persistent organ failure. Persistent organ failure may be single or multiple organ failure.

Acute Pancreatitis Work Up

In clinical practice, clinical features particularly pain abdomen, nausea, vomiting with a raised serum amylase and lipase are the diagnostic cornerstones for acute pancreatitis. The serum amylase levels usually elevate within 24 hours of the onset of symptoms and gradually returns to normal in the subsequent week. Persistently elevated serum amylase beyond the initial week of illness reflects the ongoing pancreatic inflammation or development of complications like pseudocyst or abscess.

The sensitivity of amylase at a cutoff of 300 IU/L is 91% to 100% but the specificity is low around 71% to 98%, since elevated serum levels occur in many conditions (intra-abdominal and extra-abdominal).[68] Furthermore, amylase level is not raised in 5% of cases with hyperlipidemic pancreatitis, extensive pancreatic necrosis, or chronically diseased pancreas.

Measurement of amylase isoenzyme components can improve the accuracy in the diagnosis of acute pancreatitis. P-type isoenzyme, which arises from the pancreas is more specific than the total amylase and may persist for a longer duration.

Urinary amylase levels remain elevated longer than serum levels. Furthermore, elevated serum amylase levels secondary to macro amylasemia may be detected by decreased urinary amylase levels.[69-71] Amylase–creatinine clearance ratio has also been used in the diagnosis of acute pancreatitis. This is calculated by the equation.[72]

Urine amylase/serum amylase X serum creatinine/urine creatinine

The ratio varies from 1-5%. A ratio of more than 6% is consistent with the diagnosis of acute pancreatitis. However, the amylase creatinine

clearance ratio may also be raised in diabetic ketoacidosis, burns, renal insufficiency, perforated peptic ulcer, pancreatic carcinoma, etc.

Serum lipase elevation is a more specific and sensitive indicator of acute pancreatitis than serum amylase because lipase circulating in the serum is mostly of pancreatic origin.[73] Lipase rises within 4-8 hours of the onset of pancreatitis, peaks at 24 hours, and normalizes in 8-14 days.[74] The advantage of lipase over amylase is that it is more sensitive in alcoholic pancreatitis and in patients who present 24 hours after onset of pancreatitis as lipase is elevated for longer periods.[75] The simultaneous determination of amylase and lipase offers sensitivity and specificity of 90 to 95 % for detecting acute pancreatitis in patients presenting with acute abdominal pain.

Diagnostic paracentesis[76] and analysis of peritoneal fluid for elevated amylase and lipase combined with serum elevations of the same has been strongly correlated with acute pancreatitis.

Pancreatitis can induce a diffuse capillary leak syndrome that, when combined with vomiting, can result in significant fluid losses which can lead to marked hypovolemia. This usually results in increased hematocrit, hemoglobin, blood urea nitrogen, and creatinine. Serum albumin levels may be markedly depressed, particularly if fluid loss is corrected by administration of albumin-free crystalloid solutions. The serum electrolytes may be normal, but with significant vomiting, a hypochloremic metabolic alkalosis can develop.

The white blood cell count is usually elevated with an associated left shift in the differential count. Blood glucose may be elevated either due to associated diabetes mellitus or because of increased glucagon and catecholamine release combined with diminished insulin release.

Hyperbilirubinemia is relatively common during the early stages of pancreatitis. It may be caused either by a biliary tract stone or by the inflamed (and possibly fibrotic) pancreas causing bile duct obstruction. This can result in cholangitis with positive blood cultures along with ongoing pancreatitis. The hyperbilirubinemia in pancreatitis can also

occur due to non-obstructive cholestasis that often accompanies any severe illness.

Hypertriglyceridemia is the third most common cause of AP after gallstones and alcohol. The incidence is particularly high in AP during pregnancy.[77] Hypertriglyceridemia is routinely seen in patients with hyperlipidemia induced pancreatitis. Hypertriglyceridemia can also be induced by exposure to ethanol. Serum triglyceride levels above 1000 mg/dl are usually considered necessary to ascribe causation for AP. Interestingly, an elevated cholesterol level by itself is not associated with pancreatitis.[78]

Autoimmune pancreatitis is new in the world of pancreatitis.[79] IgG4 plays a key role in the diagnosis of autoimmune pancreatitis. The cutoff used for the diagnosis is 135 mg/dl.[80]

Many patients with pancreatitis usually have hypocalcemia, which can be explained by the hypoalbuminemia that accompanies pancreatitis. Occasionally, however, patients with severe pancreatitis have decreased levels of free, ionized calcium that is not a reflection of hypoalbuminemia. This type of hypocalcemia is usually associated with a poor prognosis. Some of these patients manifest tetany and carpopedal spasm, making treatment with calcium mandatory.

In some cases of AP, thrombocytopenia, elevated levels of fibrin degradation products, a decreased fibrinogen level, prolonged partial thromboplastin time, and a prolonged prothrombin time may also be observed.

Radiological Procedures

Paralytic ileus, sentinel loop [dilate proximal jejunal loop], colon cut-off sign [distension of the colon to the level of transverse colon with no gas in the splenic flexure], obliteration of psoas margins [due to retroperitoneal irritation and pancreatic calcifications] may be observed in plain radiograph of abdomen in patients with AP.[81]

A plain radiograph may also rule out potential abdominal emergencies like perforation of hollow viscous. A chest radiograph may show left pleural effusion, elevated left hemi-diaphragm, basal atelectasis.It may also rule out other causes of pain abdomen like left lower lobe

pneumonia or pneumoperitoneum. In multi-organ failure, if the lung is affected, ARDS changes are seen on chest X-ray.[81]

Abdominal ultrasonographic evaluation of the abdomen may show increased size and decreased echogenicity of the pancreas as well as possible fluid collections.[82] The view of the pancreas is frequently obscured by overlying bowel gas from the co-existent ileus. It is the test of choice for the diagnosis of gallstones and sludge. It also detects ascites, pseudocysts, and portal or splenic vein thrombosis.[83]

Contrast-Enhanced Computed Tomography (CECT) is the imaging modality of choice. It has three major roles in the evaluation of patients with known or suspected acute pancreatitis.

- to confirm the diagnosis
- stage the severity of the inflammation process
- to detect complications, particularly parenchymal and peri-pancreatic necrosis.[81]

The CECT abdomen has been observed to have a sensitivity of 87 % and an overall detection rate of over 90 % for pancreatic gland necrosis.[84] 15 to 30 % of patients with mild disease may have normal scans.[73] CT scan also provides an alternate diagnosis in a case with a false positive elevation of enzymes.[85] CT features in acute pancreatitis include parenchymal enlargement - diffuse/focal, parenchymal edema, and non-specific findings like bowel distention, pleural effusion,mesenteric edema, peri-pancreatic changes, blurring of fat planes, thickening of the fascial plane, and presence of fluid collections/necrosis.

The removal of necrotic pancreatic tissue in the first week of an attack does not improve the survival of the patient and the delineation of the necrotic tissue is better after 4 to 5 days; therefore CT scan should be deferred for 5 to 10 days from the onset of disease. Early CT scan may be indicated when the diagnosis is in doubt or in case of blunt or penetrating injury to the abdomen.[86]

Magnetic Resonance Imaging (MRI) does not confer any major advantage over contrast-enhanced CT scan. MRI employing rapid gradient echo breath-hold technique, fat suppression, and gadolinium

intravenous administration is acceptable over other invasive alternative modalities to stage patients with acute pancreatitis. Its clinical application is reserved for patients in whom the administration of iodinated contrast material is contraindicated or to better characterize equivocal CT abnormalities.[86]

Endoscopic retrograde cholangiopancreatography (ERCP) has no role in diagnosing AP. In moderate-to-severe acute gallstone pancreatitis, therapeutic application of ERCP has been shown to lower morbidity and mortality when compared to traditional medical treatment alone by several controlled clinical trials. ERCP is also utilized in the differential diagnosis and elective treatment of recurrent unexplained pancreatitis secondary to the sphincter of Oddi dysfunction, pancreatic divisum, and microlithiasis.[87]

Prognostic Stratification

Early assessment and prediction of severity are of immense importance to avoid costly and invasive monitoring and treatment in a large group of patients who tend to turn a benign course. Accurate prediction of severity and monitoring is also important in a severe form in an intensive care unit to anticipate complications early, to consider aggressive treatment, and to judge the response to therapy.

Multifactor Scoring Systems

Many multifactor scoring systems have been described in an attempt to accurately predict the outcome of the disease.

1. Ranson’s criteria.
2. BISAP - Bedside Index for Severity of Acute Pancreatitis.
3. Glasgow (Imrie) criteria.
4. APACHE I, II, III - (Acute Physiology and Chronic Health Evaluation).
5. Balthazar’s score - depends on CT scan findings.
6. MRCS score - (Medical Research Council Sepsis).
7. SAPS - (Simplified Acute Physiology score)

Ranson’s Criteria

In 1974, Ranson developedone of the early systems for judging the severity of AP. The five initial criteria assess the severity of the acute

inflammatory process whereas the six criteria measured at 48 hours determine the systemic effects of circulating enzymes and toxins.[88]

The presence of 3 or more Ranson's signs usually indicates severe pancreatitis.

Table 4: Ranson's Criteria

1. In Alcohol-induced and other Acute pancreatitis

At admission	During the initial 48 hours
Non Gallstone pancreatitis	A decrease in PCV >10 points
Age >55 years	Increase in BUN > 5 mg/dl
WBC count > 16,000/mm3	Serum calcium < 8 mg/dl
Glucose > 200 mg/dl	Arterial PO2 < 60 mm Hg
LDH > 350 U/L	Base deficit > 4 mmol/Litres
Aspartate aminotransferase >250 U/L	Fluid sequestration > 6 Litres

2. In Gallstone pancreatitis

At admission	During the initial 48 hours
Age >70 years	A decrease in PCV >10 points
WBC count > 18,000/mm3	Increase in BUN >2 mg/dl
Glucose > 220 mg/dl	Serum calcium < 8 mg/dl
LDH >400 U/L	Base deficit >5 mmol/Litres
Aspartate aminotransferase >250 U/L	Fluid sequestration >4 Litres

Table 5: Mortality increases with the number of Ranson's signs

Criteria	Death rate
2 or < 2	<1%
3-4	16%
5 or > 5	> 40 %

BISAP Scoring System

To estimate the risk of in-hospital mortality in patients with AP, in 2008, Wu et al retrospectively developed a new scoring system, the bedside index for severity in acute pancreatitis (BISAP).[89]

Components of BISAP score:-

1. BUN> 25 mg/dl
2. Impaired mental status (Glasgow coma scale score <15)
3. SIRS (Systemic inflammatory Response Syndrome) is defined as two or more of following

- Temperature of < 36 or > 38 ° c
- Respiratory rate > 20 breaths/min or paco2 <32 mm Hg
- Pulse > 90 beats/min
- WBC < 4,000 or > 12,000 cells/mm3 or > 10% immature bands
- Age > 60 years
- Pleural effusion detected on imaging

1 point given for each variable and score calculated within 24 of diagnosis. A score of > 3 indicates severe acute pancreatitis with increased morbidity and mortality.

Modified Glasgow criteria[90]

Within 48 hours of admission

- Age >55 years
- White blood cell count > 15000/mm3
- Glucose > 180mg/dl
- Blood urea nitrogen > 45 mg/dl
- Lactate dehydrogenase > 600U/L
- Albumin < 3.2gm/dl
- Arterial oxygen pressure < 60mm Hg
- Serum calcium < 8 mg/dl

A score of ≥ 3 indicates severe pancreatitis

A limitation of the commonly used scoring systems such as Ranson's or Glasgow criteria is the need to wait for 48 hours to obtain a complete assessment. Despite refinements, the above scoring systems were found to have low sensitivity and specificity.

APACHE System

The APACHE (Acute Physiology and Chronic Health Evaluation) system was reported by Knaus and colleagues.[34] APACHE II scoring was developed in 1985 to predict the severity.

It measures 12 physiological parameters and additional points for age and underlying medical conditions. The parameters used include rectal temperature, mean arterial pressure, heart rate, respiration rate, FiO2, arterial pH, serum sodium, serum potassium, serum creatinine, hematocrit, and white cell blood count. It can be applied at the time of admission and measuring the score daily is useful to assess the progression of the disease.[91]

A score of more than or equal to 8 points predicts 11% to 18% mortality. Because obesity is a risk factor for severe disease and increased mortality, it was included in APACHE II and called APACHE-O.[92,93]

Balthazar's CT Severity Index (CTSI)

The morphological severity of acute pancreatitis can be defined precisely using the CT scan was described by Balthazar and co-workers.[94]

The severity of the acute inflammatory process is categorized into stages A to E, corresponding to scores of zero to four respectively. Secondly, the presence and extent of gland necrosis are assessed. The CT grade score is added to the necrosis score.

Table 6: Balthazar's CT severity index.[94]

CT Grade	CT Scan Description	Score
A	Normal pancreas	0
B	Enlargement of pancreas	1
C	Inflammatory changes in the pancreas and peripancreatic fat	2
D	Ill-defined single fluid collection	3
E	Two or more poorly defined fluid collections	4

Necrosis Score

Necrosis %	Score
< 30%	2
30 - 50%	4
> 50%	6

Interpretation

- 0– 3: Mortality 3%, Morbidity 8%
- 4– 6: Mortality 6%, Morbidity 35%
- 7– 10: Mortality 17%, Morbidity 92%

Drawbacks of CT scan are the expenses and its limited availability.

Single Prognostic Factors

Several clinical signs, biochemical markers, and imaging procedures have emerged in an attempt at early identification of pancreatic necrosis, monitoring of its progression, and assessment of the response to therapy.

The ideal prognostic biomarker in AP should be clinically available, inexpensive, insensitive to inter-individual differences, and accurately predict severe cases upon admission.

The search for such a biomarker is ongoing for decades and numerous promising candidates have been proposed. However, still, no marker has been able to predict complicated disease with sufficient precision. Following markers have been studied over years to predict the severity of AP.

1. Creatinine - In 2009, Muddana et al first observed that an increase in creatinine greater than 1.8 mg/dL within 48 hours of admission despite adequate hydration as a marker for the development of pancreatic necrosis. This study had a positive predictive value of 93%.[95] Later in 2010, Lankisch et al publishedthat a rise in serum creatinine does not correlate with the development of pancreatic necrosis based on a 462 patients prospective study.[96]

2. Hematocrit (Hct) - In 2000, Brown et al. observed hemoconcentration as an early marker for necrotizing pancreatitis and organ failure.[97] The cutoff value was a hematocrit of 44% at admission. The negative predictive value at 24 hours was 96% for necrotizing pancreatitis and 97% for organ failure. The admission hematocrit was comparable to the APACHE II score in predicting necrotizing pancreatitis.

3. Urinary Trypsinogen Activation Peptide (TAP) - Urinary TAP and Hematocritare not surrogate markers of inflammation, unlike other

markers. Intra-pancreatic activation of trypsin releases many protein products like TAP, trypsinogen II, and carboxypeptidase B. Out of these, TAP has been observed to be successful in predicting the severity of AP. The levels of TAP are found to be most stable in the urine. Khan et al. used a cutoff of 35 mmol/L within 12 hours of the onset of symptoms with a sensitivity of 100%, a specificity of 77%, and a negative predictive value of 100%.[98]

4. C - Reactive Protein (CRP) - Since the 1990s, CRP is a well-established marker for pancreatic necrosis and is considered the gold standard. According to the Santorini consensus conference in 1999, a cutoff of 150 mg/L done at 48 hours after the onset of symptoms has been accepted as the predictor for pancreatic necrosis.[99] CRP has been observed to have an overall accuracy of 93% and is widely available, easy to measure, and cheap to perform. The only drawback is that the peak rise of CRP is observed after a lag period of 48-72 hours from the onset of pancreatitis.[68] This is a significant amount of time because considerable damage can be done by this time.

5. Polymorphonuclear (PMN) Elastase -Neutrophils release PMN elastase, a lysosomal protease, in the inflamed pancreas. It is responsible for the activation of the complement and fibrinolytic pathway. In 1991, Uhl et al from Germany observed that the accuracy of PMN elastase was 84% with a cutoff of 120 g/L when compared to CRP at 86%.[100] The main advantage over CRP was that it reached its peak on Day 1.

6. TNF-alpha - TNF-alpha is a pleiotropic cytokine expressed in acinar cells. It plays a pivotal role in AP and binds to the soluble TNF receptor. The ability to be a clinically useful test is limited as it is rapidly cleared from the blood. THE soluble TNF receptor acts as an anti-inflammatory molecule.[101] De Beaux et al observed that the soluble TNF receptor levels were better than TNF-alpha levels in predicting severe AP from Day 1.[102]

7. IL-1 - IL-1 is a biomarker for sterile necrosis and severity of AP at admission.[103]

8. IL-6 - Macrophages release a cytokine, IL-6, which mediates the synthesis of acute-phase proteins. According to Chen et al study, IL-6 was found as a useful parameter for early prediction of the prognosis of AP.[104]It was observed to be superior to CRP and APACHE II at 24 hours. Chen et al. showed that at a cutoff of 400 pg/mL on Day 1, it has a sensitivity of 89%, a specificity of 87%, and accuracy of 88%.[104]

9. Red cell distribution width (RDW) - RDW measures the heterogeneity of size of red blood cell (RBC) in the peripheral blood, morphologically, known as anisocytosis. It is a routine parameter of the complete blood count test, described as simple, easy, inexpensive and quantitative test. RDW has been associated with inflammatory markers such as CRP, interleukin-6 and fibrinogen. Marta Gravito-Soares et al[105] conducted a retrospective study in 2018 on patients admitted with AP between 2014-2016 to find out Red cell distribution width and red cell distribution width to total serum calcium ratio as major predictors of severity and mortality in acute pancreatitis. This study concluded the good predictive power of RDW, evaluated at admission and in the first 24 h, as well as RDW0h-to-TSC ratio for both severity and mortality in AP, being superior to Ranson, BISAP, and MM scores. RDW0h > 13.0 and RDW0h-to-TSC > 1.4 were excellent predictors for AP severity. RDW0h > 14.0 and RD0h-to-TSC > 1.7 were very-good predictors for AP mortality.

Complications of Acute Pancreatitis

With improvements in supportive and intensive care, recovery from acute pancreatitis is expected but still complications occur in one third of patients, and a quarter of these may die as a result. Acute pancreatitis progresses from mild edematous to severe necrotizing acute pancreatitis and can be associated with a range of complications that could be local or systemic.

1. Local Complications
    a. Peri-pancreatic fluid collection
    b. Pancreatic phlegmon
    c. Sterile necrosis

d. Infected necrosis

e. Pancreatic pseudocyst

f. Pancreatic ascites

g. Involvement of adjacent organs with hemorrhage, thrombosis, bowel infarction, obstructive jaundice, fistula formation, or mechanical obstruction.

2. Systemic Complications

A. Pulmonary

I. Pneumonia, atelectasis

II. Acute respiratory distress syndrome - ARDS may occur within few days of admission or after the development of infected necrosis and septicemia. It occurs due to the release of activated pancreatic enzymes, vasoactive lysosomal enzymes, and especially phospholipase A2 (which destroys surfactant).

III. Pleural effusion

IV. Tachypnea, mild respiratory alkalosis, and mild hypoxemia are common within two days of the onset of acute pancreatitis.

These clinical features can be managed with analgesia, supplemental oxygen, and chest physiotherapy. If pleural effusion develops, it may require intercostal tube drainage. Impending respiratory failure is suggested when the arterial PO2 remains <60 mm Hg despite high-flow oxygen by mask and such patients are considered for mechanical ventilation.

B. Cardiovascular

I. Hypotension

II. Hypovolemia - From third-space, fluid loss is common within the first 12 hours and maybe upto 30% in severe acute pancreatitis. It should be anticipated with aggressive intravenous fluid therapy in the first 24 to 48 hours.

III. Cardiac failure (MAP<70 mm Hg) requires prompt aggressive fluid resuscitation with or without inotropic support.

IV. SIRS causes decreased peripheral vascular resistance and preferred use of norepinephrine to increase vascular tone and blood pressure (dose0.05 to 0.2 µg/Kg/min).

V. Pericardial effusion

C. Hematologic

I. Hemoconcentration

II. Disseminated intravascular coagulopathy

D. GI hemorrhage

I. Peptic ulcer

II. Erosive gastritis

III. Portal vein or splenic vein thrombosis with varices

E. Renal -

I. Renal impairment occurs due to both hypovolemia (pre-renal failure) and direct nephrotoxicity from mediators of acute pancreatitis. Activation of the renin-angiotensin system may also contribute to decreased renal perfusion.

II. Oliguria (<30 ml/hour)

III. Azotemia

IV. Renal artery/vein thrombosis

The initial approach is aggressive intravenous crystalloid administration (up to 10 Liters /24 hours). Diuretics (furosemide 20-200 mg/24hour) and dopamine infusion(4 µg /kg/min) should be considered. Further deterioration may require hemodialysis.

F. Metabolic

I. Hyperglycemia - It may occur due to a stress-induced increase in cortisol and catecholamines, hyperglucagonemia and insulin deficiency due to necrosis of islet cells. It is a poor prognostic sign.

II. Hypocalcemia -It occurs as calcium is sequestered in areas of fat necrosis by the process of saponification. And due to altered calcium regulating hormones (calcitonin, PTH, and glucagon).

III. Hypertriglyceridemia

IV. Encephalopathy

V. Sudden blindness (Purtscher’s retinopathy)

G. Central nervous system

I. Psychosis

II. Fat emboli

III. Alcohol withdrawal syndrome

H. Fat necrosis

I. Intra-abdominal saponification

II. Subcutaneous tissue necrosis

Treatment of Acute Pancreatitis

All cases of acute pancreatitis should be stratified into mild, moderately severe, and severe during the first 48 hours using one of the scoring systems. Mild cases can be managed in the ward with noninvasive monitoring. Severe cases need intensive monitoring and resuscitation in ICU. The patient should be referred to a specialized center depending on the local resources available and the patient's condition.

Medical Treatment

The initial management of AP is mainly non-operative and supportive. The initial management of the patient includes fluid replacement, electrolyte balance, pain management, nutritional support, and prevention and treatment of local and systemic complications.[87,106,107]

Factors that may have caused pancreatitis such as alcohol or drugs are to be avoided. Hemoconcentration and hypovolemia may be caused due to enormous fluid losses. External fluid losses like repeated vomiting and nausea further limit fluid intake. Internal fluid losses are caused by fluid sequestration into third spaces. This occurs due to the diffuse capillary leak phenomenon triggered by pro-inflammatory factors.[87,106,107]

These losses should be replaced by crystalloids and colloids to maintain a CVP of 8 - 12 cms of water. Hourly monitoring of urine output, CVP, arterial BP, O2 saturation should be done in severe cases. Potassium, Calcium, Magnesium should be closely monitored and deficiency replaced. Glucose levels of more than 250ml/dl necessitate insulin administration.[87]

In case of hematocrit less than 25%, a blood transfusion is indicated. Periodic assessment of arterial blood gas for acidemia is required for severe cases. Pain in acute pancreatitis is so severe that it usually requires parenteral analgesics. Narcotics are the therapy of choice. There is no definitive human study to support that morphine exacerbates pancreatitis by contracting Sphincter of Oddi.[108]

Nasogastric tubes were routinely placed in the past to remove gastric secretion. However, three randomized trials showed no clear benefit in its empiric use.[87,106,107]

Severe acute pancreatitis is associated with a cytokine-mediated systematic inflammatory response and a hypercatabolic state.[109] Protein-calorie malnutrition, expansion of the extracellular fluid compartment, and immune suppression are the adverse consequences of AP. A meta-analysis of RCTs showed that nutritional support, both enteral and parenteral, significantly loweredthe risk of mortality in patients with acute pancreatitis compared with no nutritional support.[110] Thus nutritional support is an integral part of patient care in patients with AP.[111,112]

Several RCTs compared total PN and total EN in the management of predicted severe AP.[113-120] A meta-analysis of high-quality RCTs has shown a significant two-fold reduction in the risk of total and pancreatic infectious complications and a 2.5 fold reduction in the risk of death in patients receiving total enteral nutrition. Nasogastric (NG) tube insertion may be more practically used than nasojejunal (NJ), as NJ often requires endoscopy or radiology expertise, the transfer of patients within the hospital, and a delay in starting feeding. However, NJ EN has been most preferred to NG EN because of a fear of pancreatic stimulation.

Role of prophylactic antibiotics: Infectious complications are considered as the leading cause of mortality in severe pancreatitis. In about 30% of cases, polymicrobial infections tend to occur. Anaerobes account for only 10% of all pancreatic infections. Patients with fungal infections tend to have a worse outcome than those with a bacterial infection.[121] Studies on the penetration of antibiotics into necrotic tissue observedgood infusibility of Ciprofloxacin, Metronidazole, and Imipenem. Against an optimal efficacy factor of 100, Imipenem had an efficacy factor of 98 followed by Ofloxacin, Ciprofloxacin, and Piperacillin.[121]

Role of ERCP in Gallstone Pancreatitis: The leading cause of acute pancreatitis in many western and Asian countries is gall stones. The Working Party Report has given the following guidelines.[122]

1. Urgent ERCP should be performed in patients with acute pancreatitis of suspected or proven gall stone etiology when criteria for severity are met and/or there is coexistent cholangitis, jaundice, dilated CBD; or when there is clinical deterioration in patients with initial mild prognostic signs.
2. Endoscopic sphincterotomy is recommended in patients with severe gallstone pancreatitis with significant local and/or systemic complications; dilated bile duct without demonstrable stones; and a gall bladder containing stones if cholecystectomy is neither possible nor contemplated.

Surgical Treatment

The operative procedures include the following:[123]

1. Necrosectomy
    - o Re-laparotomy at intervals
    - o Open or Closed packing
    - o Continuous closed cavity lavage
2. Percutaneous drainage
3. Endoscopic (Minimally invasive) procedures
4. Cholecystectomy.

There is increasing evidence that continued conservative therapy can manage sterile pancreatic necrosis. Some believe that surgical intervention should be considered if there is no stabilization or improvement with full supportive intensive care therapy.[87]

The rationale for surgical debridement of infected pancreatic necrosis is based on several factors.[123]

1. Bacteria and their toxins are released into circulation by infected pancreatic tissue which accounts for remote organ failure.
2. Late complications such as pancreatic abscess can be prevented by removing the infected debris.
3. Continuous drainage can be provided.

4. Viable pancreatic tissue should be preserved to achieve good long-term results concerning endocrine and exocrine function.

Early diagnosis of infection in a necrotic pancreas, which significantly increases mortality, is important. In 20-55% of patients with pancreatic abscess, CT scan shows an ‘air bubble’ pattern but this is not usually seen in patients with intrapancreatic necrosis. When a patient has clinical evidence of sepsis (usually after 7 days of onset) unexplained by normal microbiology studies, a CT or USG guided FNA with immediate gram stain & subsequent culture of fluid should be done.[124]

This procedure is safe and reliable with a sensitivity and specificity of 88% and 90% respectively.[125] If there is evidence of infection, active intervention to remove the pus and adjacent peri-pancreatic or pancreatic necrosis is required. Traditionally an anterior open surgical approach has been advocated to remove the necrotic tissue using digital dissection or gentle instrumentation. If necrotic material is still present, re-laparotomy can bedone at planned intervals. The main abdominal wound can be left open (laparostomy) or closed temporarily (closed laparostomy) using a zipper, gortex, marlex, or nylon mesh.[123] When there is no bleeding and very less necrotic tissue is left behind a closed cavity continuous lavage can be done with strategically placed drains.

Alternative methods of debridement of pancreatic necrotic material have recently been described, but they require considerable technical expertise.[126] Aggressive irrigation and drainage through large-bore percutaneous catheters up to 28 French in diameter has been described. Endoscopic placement of several transgastric or transduodenal discharge catheters and nasopancreatic irrigation tube (7F) into the retroperitoneum through tracts dilated up to 15 mm has been used as another alternative.[123]

Laparoscopic or open cholecystectomy should be offered to all patients with biliary pancreatitis having a mild disease once the pain decreases. However, laparoscopic cholecystectomy during the first week of admission has been associated with an increase in operative complications, an increased rate of conversion, and a longer

postoperative stay.[125,127] Patients with severe pancreatitis should undergo cholecystectomy during necrosectomy or 2-3 weeks after the attack settles.

Prognosis of the disease

Studies have observed that the majority of patients with severe acute pancreatitis show persistent exocrine insufficiency up to 2 years. The long term clinical endocrine and exocrine consequences of acute pancreatitis depend on the following factors: -

1. Severity of necrosis
2. Cause (alcohol or non-alcoholic)
3. Whether the patient continues to consume alcohol
4. Degree of surgical pancreatic debridement.

Follow up pancreatography frequently reveals obstructive pancreatic ductal abnormalities that may account for persistent symptoms of abdominal pain or recurrent pancreatitis.[128,129]

MATERIALS AND METHODS

SOURCE OF DATA

Patients who were admitted to Dayanand Medical College and Hospital, Ludhiana with AP from 1st January, 2019 to 31st December, 2019

METHOD OF COLLECTION OF DATA

Variables evaluated included age, gender, co-morbidities, smoking habits, alcohol consumption, AP etiology, organ failure and local/systemic complications AP-associated. Biochemical tests included routine investigations done in a patient with AP such as serum calcium levels along with hematological tests like RDW as a part of complete blood count in first 24 hours of admission. In addition, data of treatment provided i.e medical or invasive (PCD or necrosectomy) and patients who expired as a result of AP was collected.

INCLUSION CRITERIA

- Age over 18 years
- Minimum hospital stay of 24 hours
- Cases presenting within 5 days of onset of symptoms
- A diagnosis of AP according to the RAC (at least two criteria: typical clinical presentation including acute persistent abdominal pain, serum amylase exceeding 3 times the upper limit of normal (100 IU/L) and characteristic findings on abdominal ultrasonography and/or computed tomography).
- AP severity was also defined according to the RAC, based on the presence of single or multiple persistent organ failure (> 48 h) and/or local complications.
- Organ failure was classified according to MM including cardiovascular, respiratory and renal failures.

EXCLUSION CRITERIA

- Factors affecting RDW, such as infectious or immunosuppressive conditions/therapy, active malignancy, chronic use of erythropoietin, recent transfusion history, pregnancy or trauma.
- Factors affecting TSC, such as parathyroid disorders, malignancies, use of thiazides or granulomatous disorders like sarcoidosis

DURATION OF STUDY

This study was conducted at DMCH, Ludhiana from 1st January, 2019 to 31st December, 2019.

OUTCOME

This study evaluated the role of RDW and ratio of RDW to TSC as predictors of outcome and in-hospital intervention required in patients diagnosed with AP.

STATISTICAL ANALYSIS

Data was described in terms of range; mean ± standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. Comparison of quantitative variables between the study groups was done using Student t-test and Mann Whitney U test for independent samples for parametric and non-parametric data respectively. For comparing categorical data, Chi square ($\chi 2$) test was performed and exact test was used when the expected frequency was less than 5. Sensitivity, specificity, positive and negative predictive values and accuracy of each method and its confidence interval (95% CI) was determined, besides the Youden index (probability of correct classification) and determining the area under the ROC curve. A probability value (p value) less than 0.05 was considered statistically significant. All statistical calculations were done using SPSS (Statistical Package for the Social Science) SPSS 21 version statistical program for Microsoft Windows.

OBSERVATIONS AND RESULTS

This study was conducted on 94 patients who were diagnosed as a case of acute pancreatitis admitted in Dayanand Medical College and Hospital, Ludhiana from 1st January 2019 to 31st December 2019. Following results were obtained from the collected data obtained within 24 hours of hospitalization.

DEMOGRAPHIC DATA-

AGE -

The mean age observed was 43.32 years. Most of them belonged to the age group of 31-40 years (25.5%) followed by <30 years (24.5%). Patients with mild pancreatitis had a mean age of 40.93±12.98 years, those with moderately severe pancreatitis had a mean age of 44.77±17.69 years while with severe pancreatitis had a mean age of 46.17±15.44 years (p-value-0.335 which is insignificant).

Table 7- Prevalence of acute pancreatitis in various age groups

Age group (years)	No. of cases	Percentage
< 30	23	24.5%
31-40	24	25.5%
41-50	17	18.1%
51-60	17	18.1%
> 60	13	13.8%
Total	94	100.0%

Table 8 - Mean age among study group according to the severity of pancreatitis

	MILD (n=44)		MODERATELY SEVERE (n=26)		SEVERE (n=24)		F	p-value
	Mean	SD	Mean	SD	Mean	SD		
Age (years)	40.93	12.98	44.77	17.69	46.17	15.44	1.107	0.335

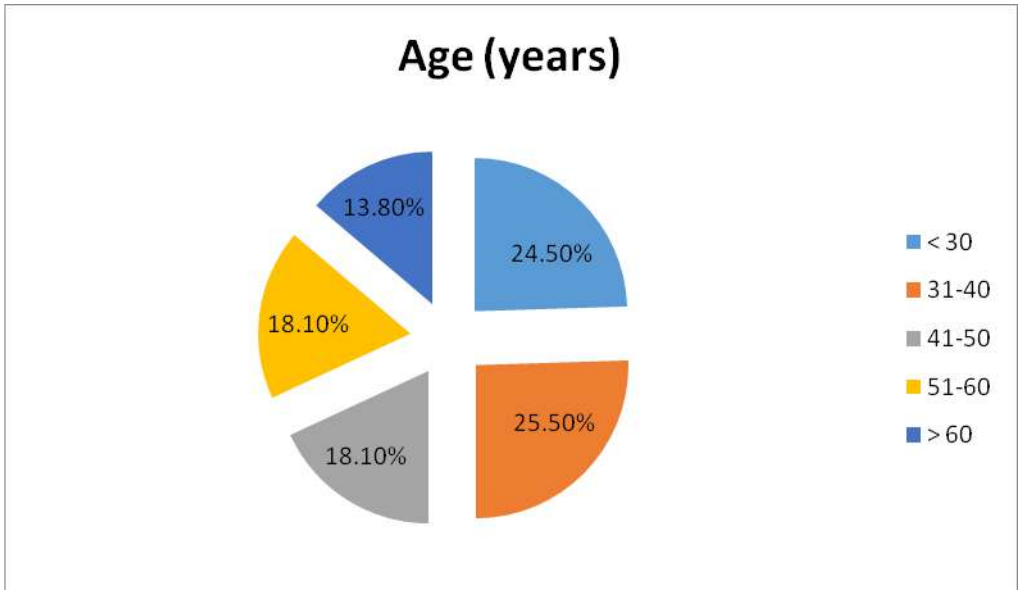

Fig 3- Prevalence of acute pancreatitis in various age groups

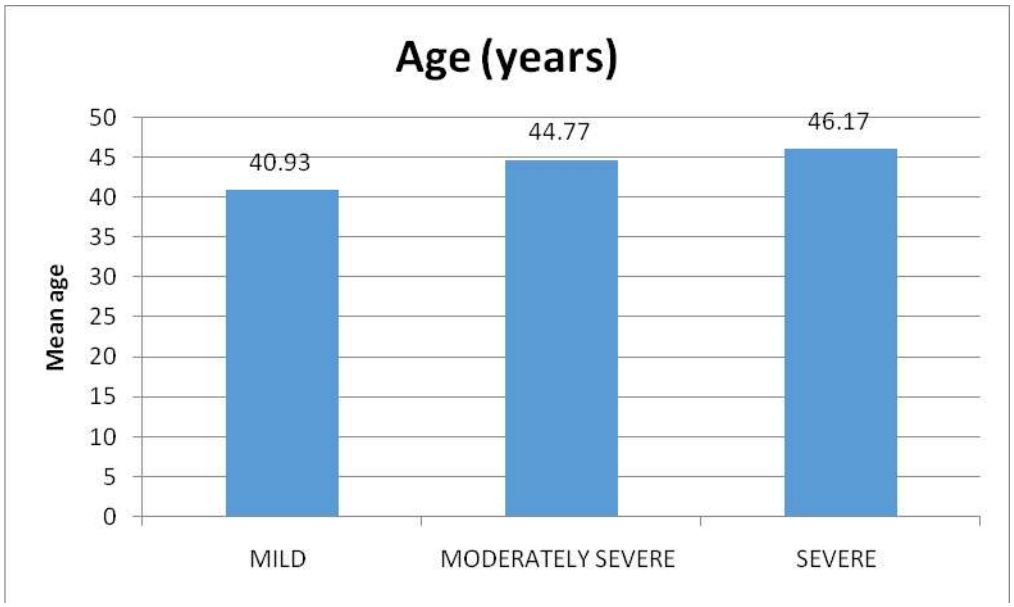

Fig 4 - Mean age among study group according to the severity of pancreatitis

SEX -

Most of the patients (63.8%) were males while 36.2% were females.

Table 9 - Gender wise distribution of acute pancreatitis

Sex	No. of cases	Percentage
FEMALE	34	36.2%
MALE	60	63.8%
Total	94	100.0%

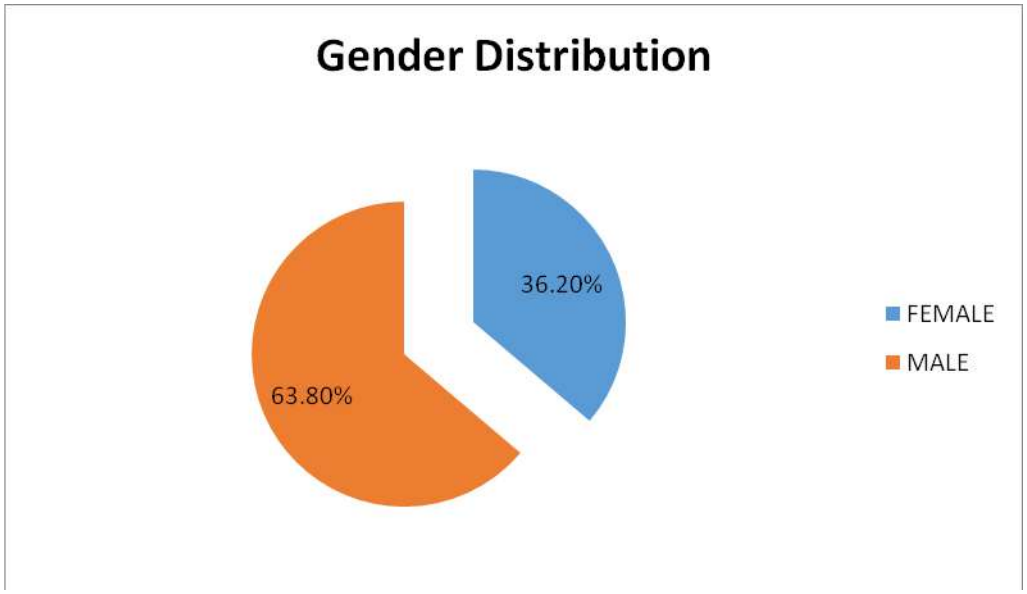

Fig 5 - Gender wise distribution of acute pancreatitis

SYMPTOMS OF ACUTE PANCREATITIS -

In our study, the most common symptom in patients with acute pancreatitis was pain abdomen (98.9%) followed by vomiting (37.2%).

Table 10 - Symptoms of acute pancreatitis among the study group

Chief Complaints	No. of cases	Percentage
Pain Abdomen	93	98.90%
Vomiting	35	37.20%
Breathlessness	19	20.20%
Fever	6	6.40%

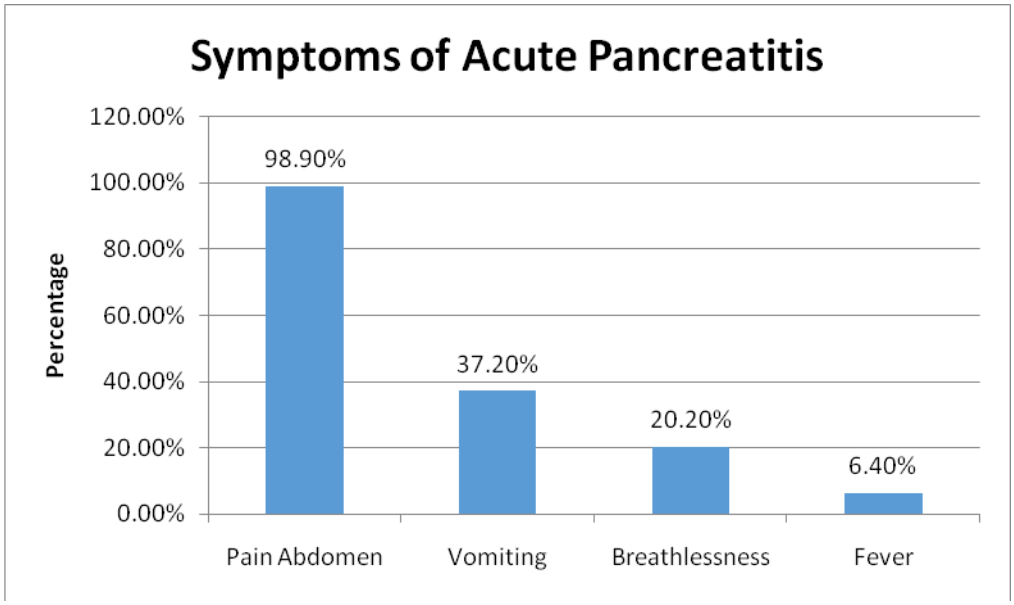

Fig 6 - Symptoms of acute pancreatitis among the study group

ETIOLOGY -

In our study, the most common cause of acute pancreatitis was biliary (46.8 %) followed by alcohol (34.0%).

Table 11 - Distribution of acute pancreatitis on basis of etiology

Etiology	No. of cases	Percentage
BILIARY	44	46.80%
ALCOHOL	32	34.00%
IDIOPATHIC	11	11.70%
POST ERCP	3	3.20%
DRUG	2	2.10%
AUTOIMMUNE	1	1.10%
TRAUMA	1	1.10%
Total	94	100.00%

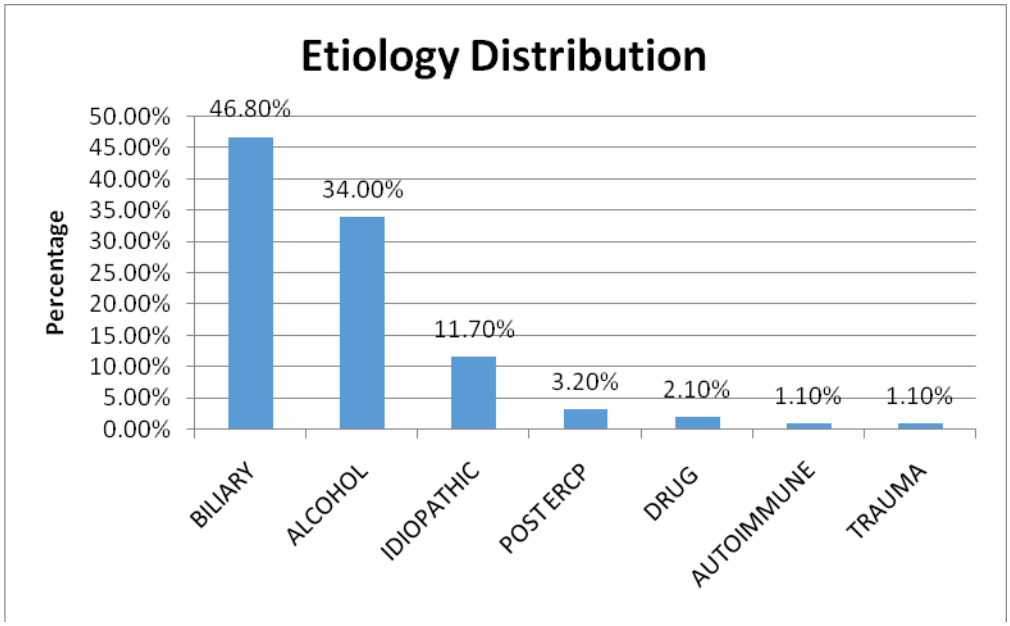

Fig 7 - Distribution of acute pancreatitis on basis of etiology

ORGAN FAILURE -

In our study, 53.2% of patients had organ failure. 47.9% had respiratory failure, 10.6% had renal failure and 4.3% had cardiovascular failure.

Table 12 - Incidence of organ failure among the study group

Organ Failure	No. of cases	Percentage
YES	50	53.2%
NO	44	46.8%
Total	94	100.0%

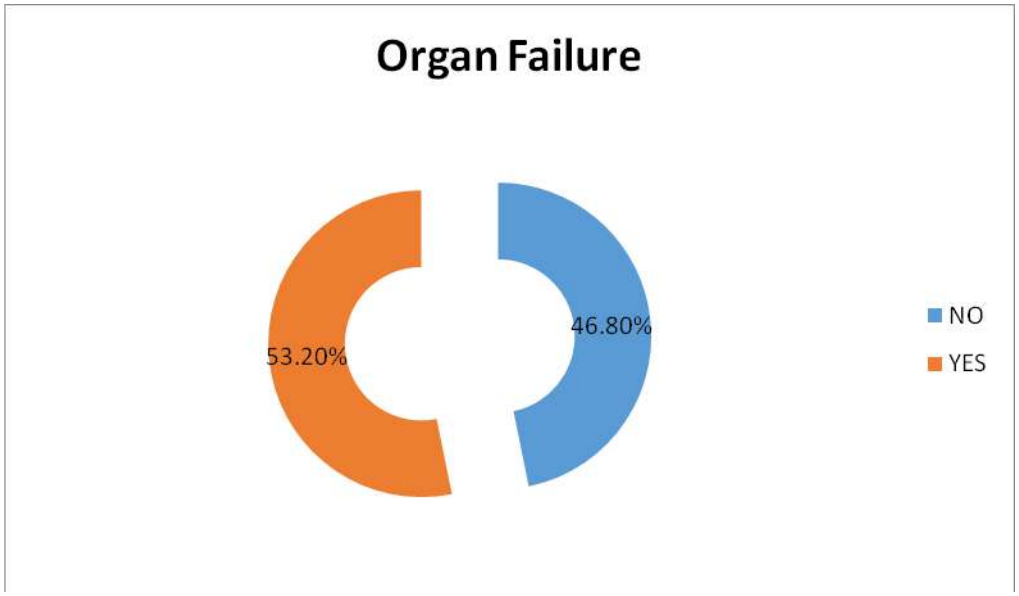

Fig 8 - Incidence of organ failure among the study group

Table 13 - Incidence of respiratory failure among the study group

Respiratory Failure	No. of cases	Percentage
NO	49	52.1%
YES	45	47.9%
Total	94	100.0%

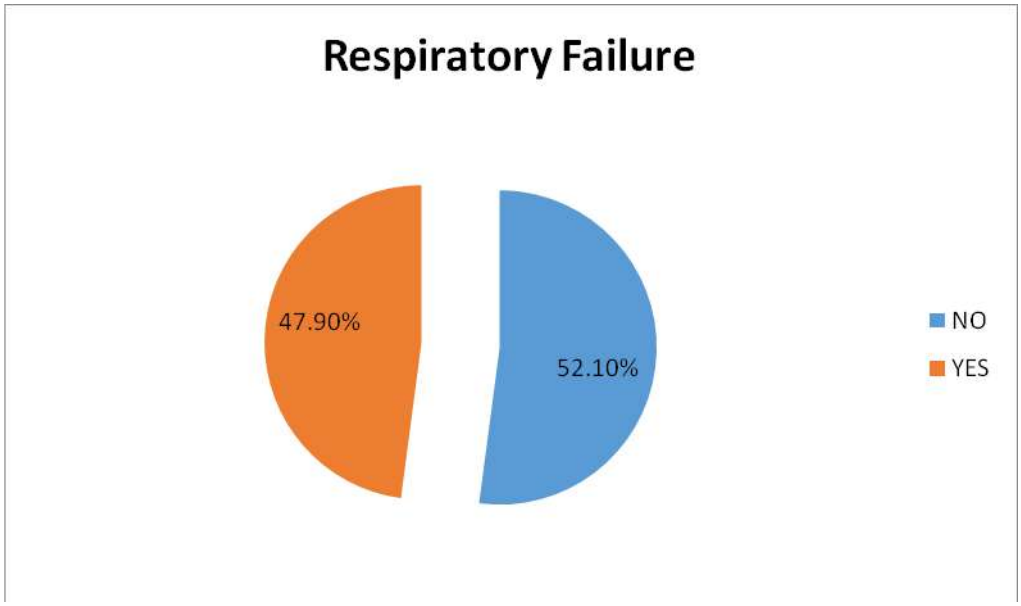

Fig 9 - Incidence of respiratory failure among the study group

Table 14 - Incidence of renal failure among the study group

Renal Failure	No. of cases	Percentage
NO	84	89.4%
YES	10	10.6%
Total	94	100.0%

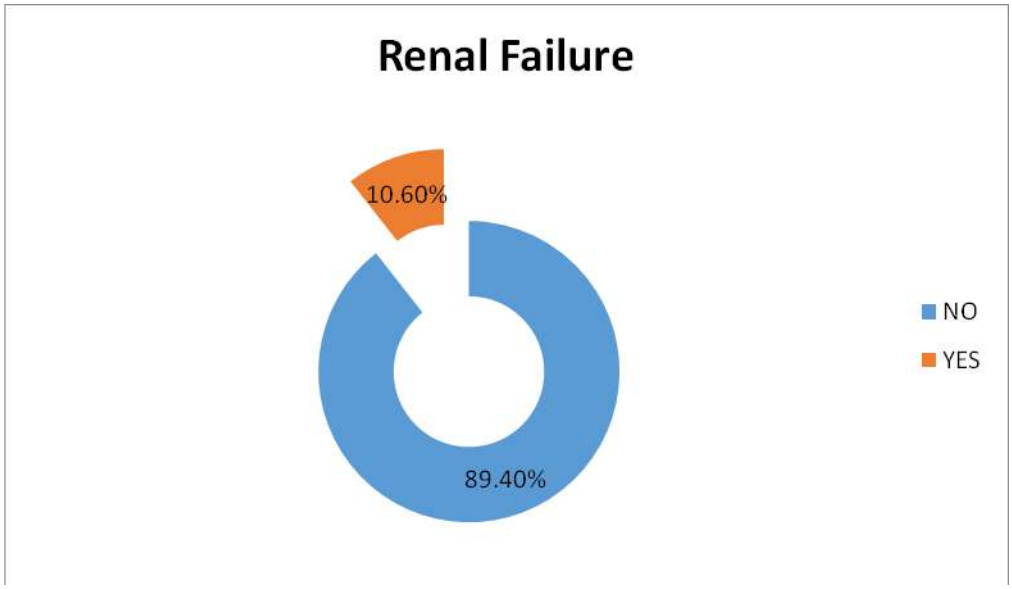

Fig 10 - Incidence of renal failure among the study group

Table 15 - Incidence of cardiovascular failure among the study group

Cardiovascular failure	No. of cases	Percentage
NO	90	95.7%
YES	4	4.3%
Total	94	100.0%

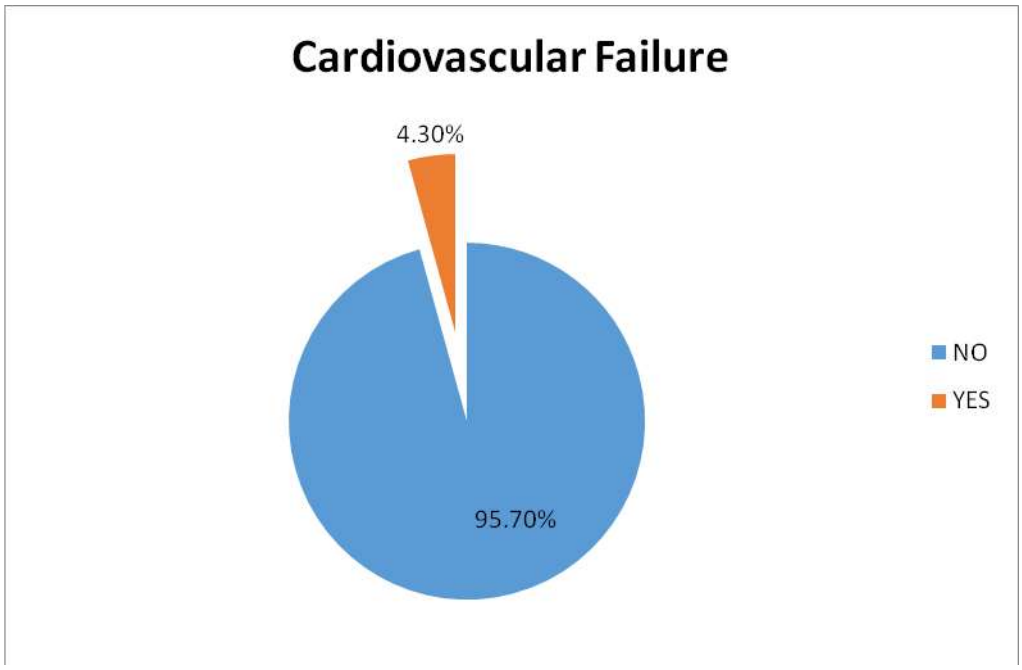

Fig 11 - Incidence of cardiovascular failure among the study group

DISTRIBUTION OF CASES ACCORDING TO REVISED ATLANTA CLASSIFICATION -

In our study, 46.8% of patients had mild pancreatitis, 27.7% had moderately severe pancreatitis while 25.5% had severe pancreatitis.

Table 16 - Distribution of cases according to revised Atlanta classification

Type of Pancreatitis	No. of cases	Percentage
MILD	44	46.8%
MODERATELY SEVERE	26	27.7%
SEVERE	24	25.5%
Total	94	100.0%

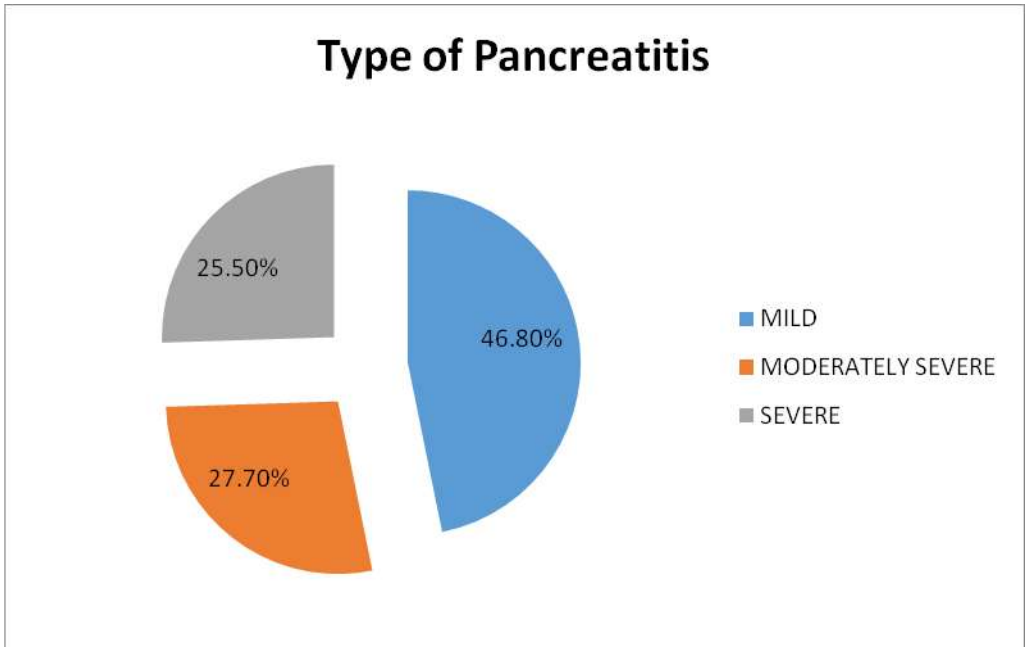

Fig 12 - Distribution of cases according to revised Atlanta classification

HOSPITAL STAY -

In our study, the average hospital stay duration for patients with mild, moderately severe, and severe pancreatitis was 8.39±3.31 days, 14.92±3.85 days, and 23.79±13.98 days respectively with a p-value - 0.000 which is significant.

Table 17 - Duration of hospital stay among study group according to Revised Atlanta classification

	MILD (n=44)		MODERATELY SEVERE (n=26)		SEVERE (n=24)		F	p-value
	Mean	SD	Mean	SD	Mean	SD		
Hospital stay (days)	8.39	3.31	14.92	3.85	23.79	13.98	31.607	0.000

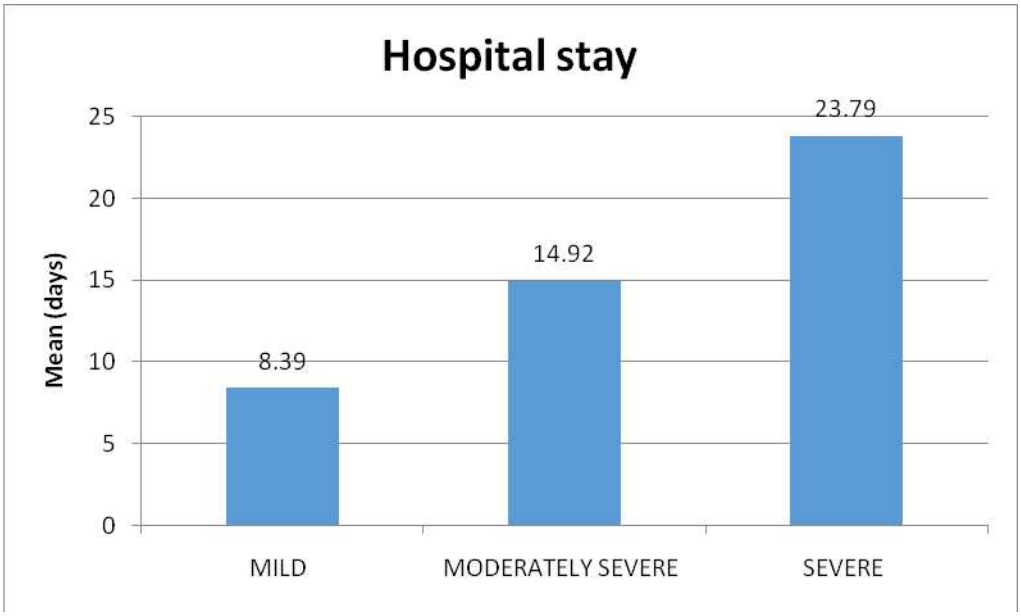

Fig 13 - Duration of hospital stay among study group according to Revised Atlanta classification

CORRELATION OF RDW AND RDW: TSC TO SEVERITY OF ACUTE PANCREATITIS -

In our study, Mean RDW for mild, moderate and severe pancreatitis was 13.36±0.72%, 15.49±0.72% and 17.86±1.14% respectively with p value 0.000 (significant) while mean RDW:TSC came out to be 1.60±0.12, 2.13±0.10, 2.88±0.27 for mild, moderate and severe pancreatitis respectively with significant p value (0.000). RDW (AUROC: 0.997; p - 0.000 i.e. significant) and RDW-to-TSC ratio (AUROC:1; p-0.000 i.e significant) were major predictors of severe AP to a cut-off value of 16.25% (Senstivity-100%; Specificity-97.1%) and 2.42 (Senstivity-100%; Specificity-100%) respectively.

Table 18 - Correlation of RDW, Serum Calcium and RDW: TSC to severity of acute pancreatitis

	MILD (n=44)		MODERATELY SEVERE (n=26)		SEVERE (n=24)		F	p-value
	Mean	SD	Mean	SD	Mean	SD		
RDW (%)	13.36	0.72	15.49	0.72	17.86	1.14	223.159	0.000
Serum Calcium (mg/dl)	8.34	0.64	7.26	0.53	6.23	0.67	93.702	0.000
RDW:TSC	1.60	0.12	2.13	0.10	2.88	0.27	459.418	0.000

Table 19- Area under the receiver operating characteristic curve (AUROC) of RDW and RDW: TSC for acute pancreatitis severity

Test Result Variable(s)	Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval		Positive if Greater Than or Equal To[a]	Sensitivity	1 - Specificity
				Lower Bound	Upper Bound			
RDW (%)	0.997	.003	.000	.000	1.000	16.25	1.000	.029
RDW:TSC	1	.000	.000	.000	1.000	2.42	1.000	.000

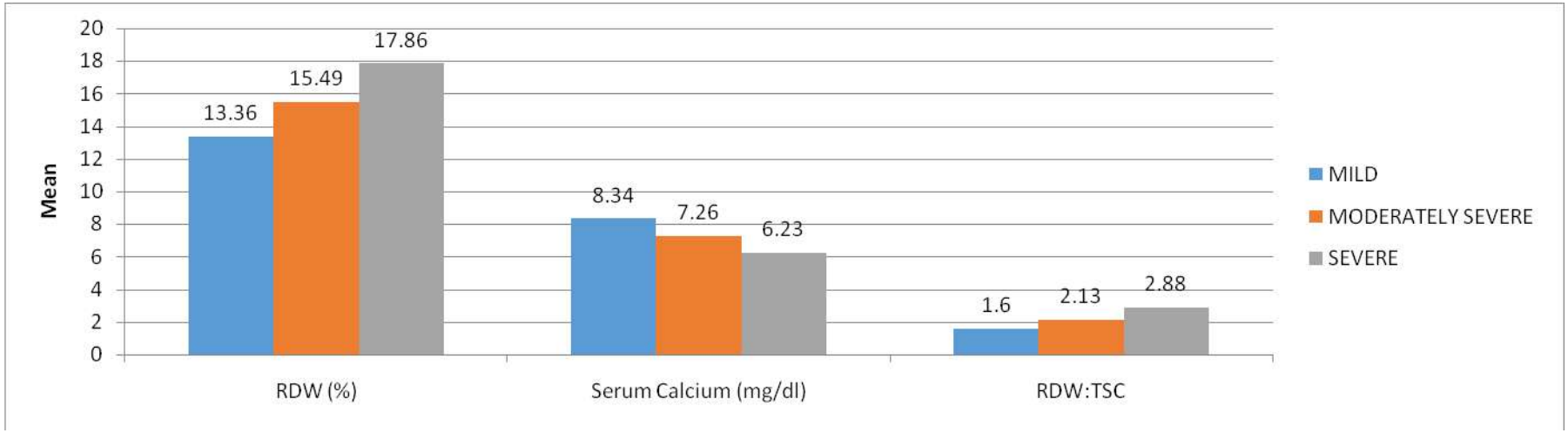

Fig 14 - Correlation of RDW, Serum Calcium and RDW:TSC to severity of acute pancreatitis

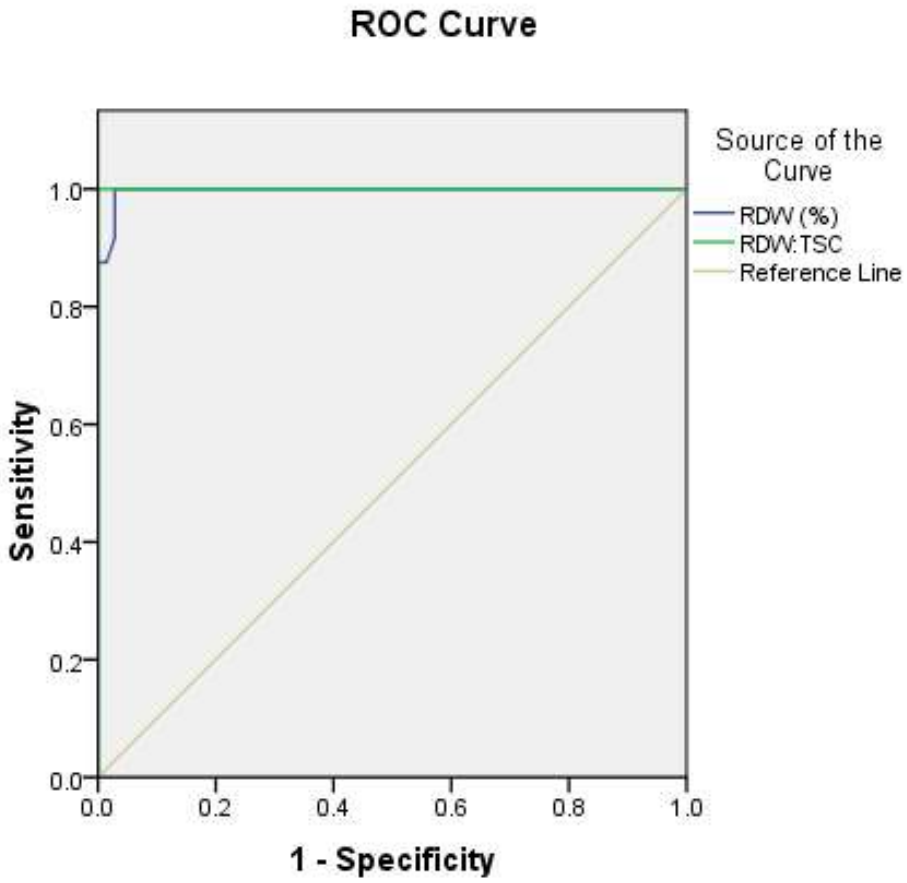

Fig 15 - Area under the receiver operating characteristic curve (AUROC) of RDW and RDW: TSC for acute pancreatitis severity

CORRELATION OF RDW AND RDW:TSC WITH MORTALITY IN ACUTE PANCREATITIS -

In our study, the mean RDW for survivors was 14.84±1.88% and for non-survivors was 18.29±0.86% with p-value 0.000 (significant) while RDW:TSC came out to be 1.99±0.49 and 3.05±0.12 for survivors and non-survivors respectively with significant p-value (0.000). RDW (AUROC:0.947; p-0.000 i.e significant) and RDW-to-TSC ratio (AUROC:0.975; p-0.000 i.e significant) were major predictors of mortality in AP to a cut-off value of 17.20% (Senstivity-100%; Specificity-87.4%) and 2.9 (Senstivity-100%; Specificity-96.6%) respectively.

Table 20 - Correlation of RDW, Serum Calcium and RDW:TSC to the mortality of acute pancreatitis

	Survival		Non-Survival		t/Z	p-value
	Mean	SD	Mean	SD		
RDW (%)	14.84	1.88	18.29	0.86	-4.793	0.000
Serum Calcium (mg/dl)	7.62	1.01	5.99	0.12	4.245	0.000
RDW:TSC	1.99	0.49	3.05	0.12	-5.631	0.000

Table 21- Area under the receiver operating characteristic curve (AUROC) of RDW and RDW:TSC for acute pancreatitis mortality

Test Result Variable(s)	Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval		Positive if Greater Than or Equal To[a]	Sensitivity	1 - Specificity
				Lower Bound	Upper Bound			
RDW (%)	.947	.023	.000	.902	.993	17.20	1.000	.126
RDW:TSC	.975	.016	.000	.000	1.000	2.90	1.000	.034

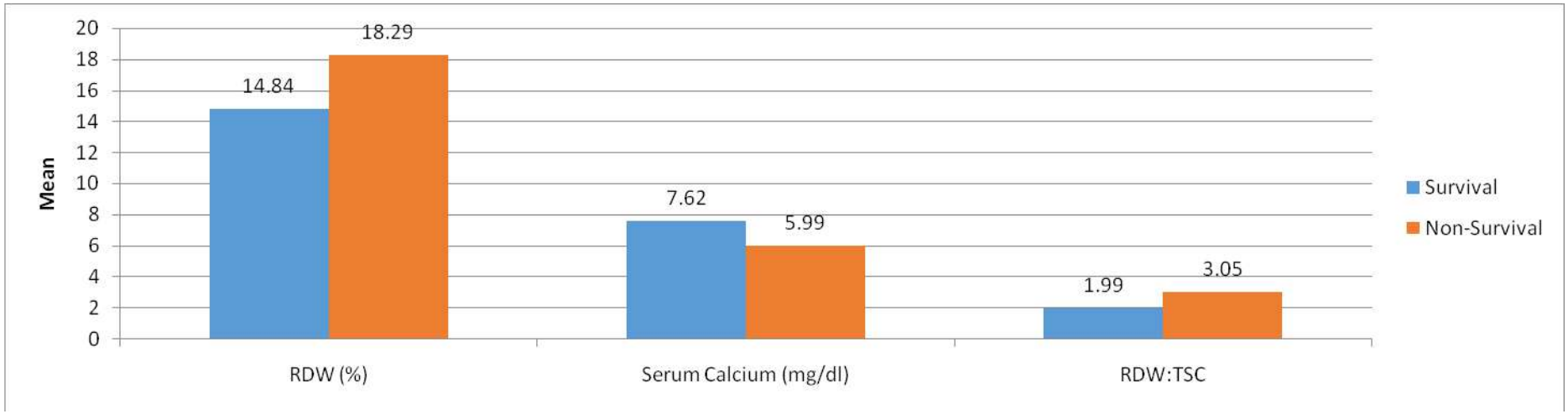

Fig 16 - Correlation of RDW, Serum Calcium and RDW:TSC to the mortality of acute pancreatitis

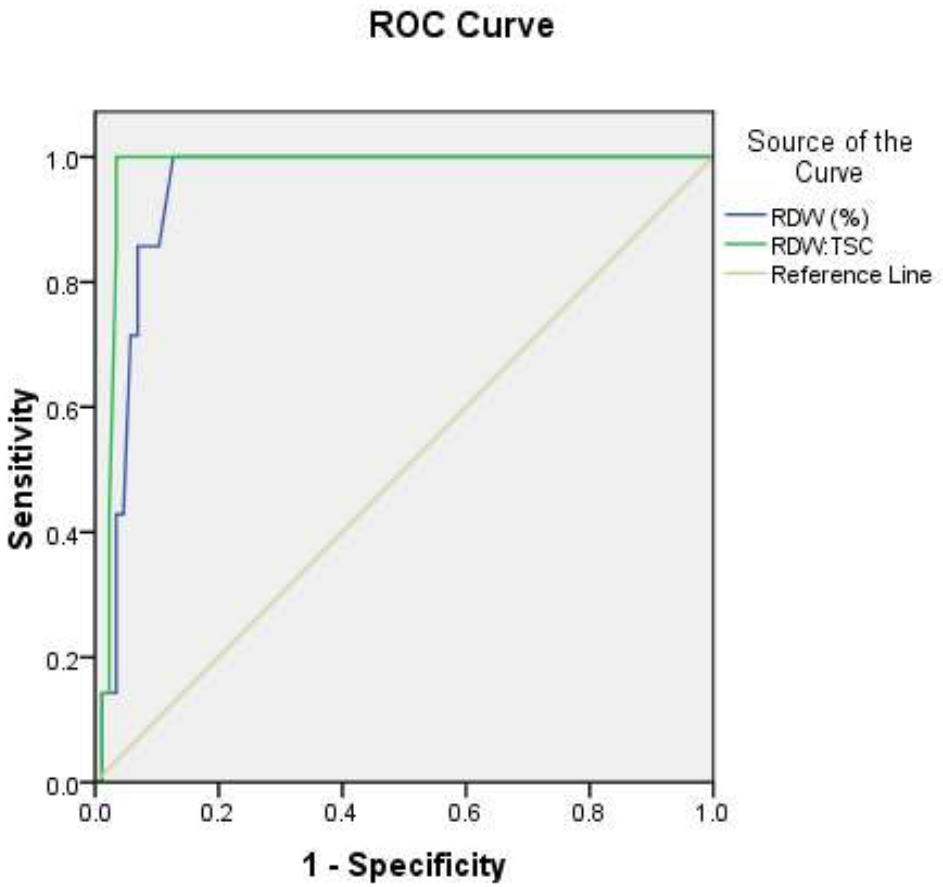

Fig 17- Area under the receiver operating characteristic curve (AUROC) of RDW and RDW:TSC for acute pancreatitis mortality

INTERVENTION -

In our study, 7.4% of patients required Per-cutaneous drainage of peripancreatic collection, 6.4% patients required pancreatic necrosectomy while only 1.1% patients required endoscopic nasocystic drainage. Mean RDW for patients requiring endoscopic nasocystic drainage, pancreatic necrosectomy, and percutaneous drainage of peripancreatic collection was 14.20 %, 17.38±0.685%, and 17.59±2.335% respectively while RDW:TSC requiring nasocystic drainage, pancreatic necrosectomy and percutaneous drainage of peripancreatic collection were 2.21, 2.83±0.201 and 2.56±0.384 respectively.

Table 22 - Incidence of different types of interventions among the study group

Intervention	No. of cases	Percentage
NO	80	85.10%
PER-CUTANEOUS DRAINAGE	7	7.40%
NECROSECTOMY	6	6.40%
NASOCYSTIC DRAINAGE	1	1.10%

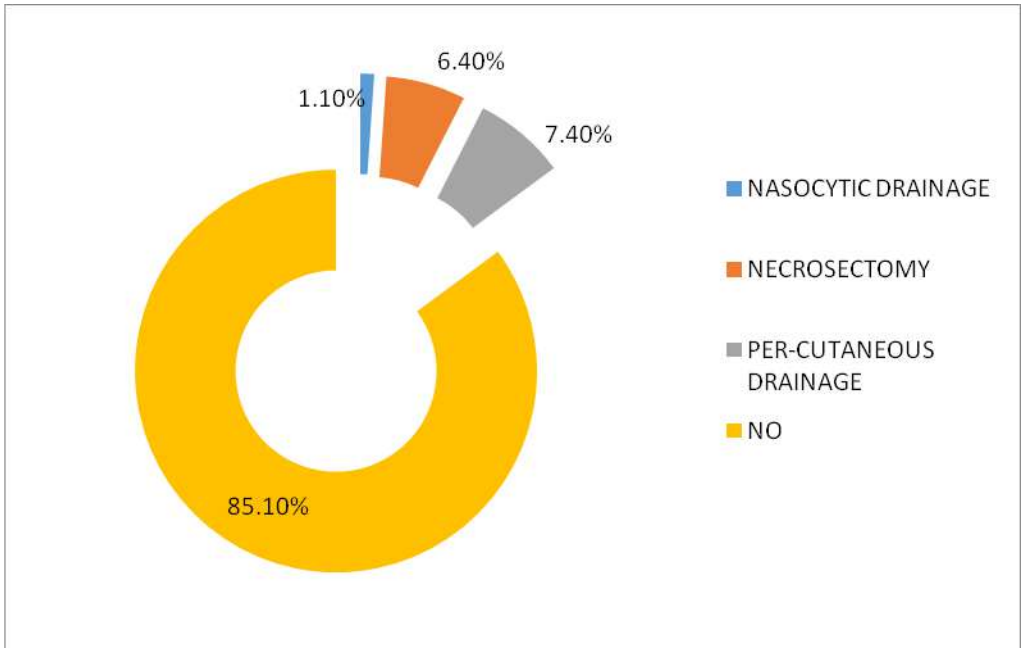

Fig 18 - Incidence of different types of interventions among the study group

Table 23 - Correlation of RDW and RDW:TSC with different types of interventions among the study group

Test Result Variable(s)	Intervention	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
						Lower Bound	Upper Bound		
RDW:TSC	No	80	1.97	.519	.058	1.86	2.09	1	4
	Nasocystic drainage	1	2.21	.	.	.	.	2	2
	Necrosectomy	6	2.83	.201	.082	2.62	3.04	3	3
	Percutaneous drainage	7	2.56	.384	.145	2.21	2.92	2	3
	Total	94	2.07	.552	.057	1.96	2.19	1	4
RDW (%)	No	80	14.72	1.824	.204	14.31	15.13	12	20
	Nasocystic drainage	1	14.20	.	.	.	.	14	14
	Necrosectomy	6	17.38	.685	.280	16.66	18.10	16	18
	Percutaneous drainage	7	17.59	2.335	.882	15.43	19.75	15	22
	Total	94	15.10	2.034	.210	14.68	15.51	12	22

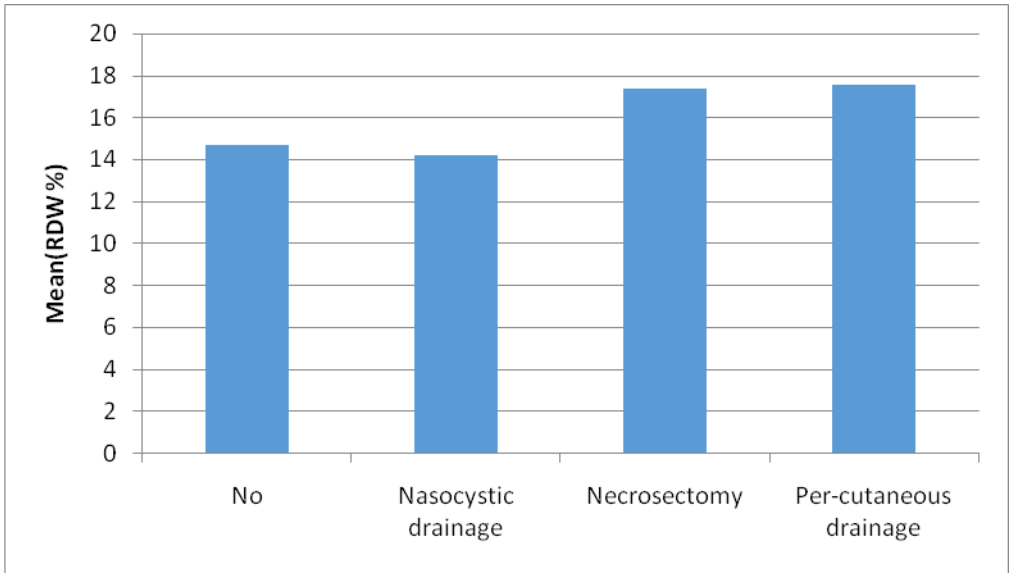

Fig 19 - Correlation of RDW with different types of interventions among the study group

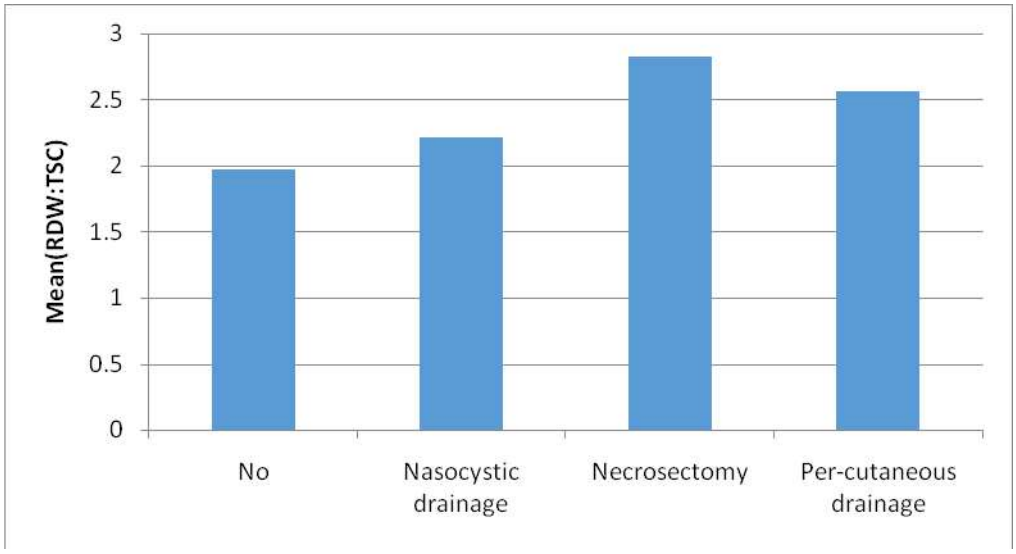

Fig 20 - Correlation of RDW:TSC with different types of interventions among the study group

OUTCOME -

In our study, 7 out of 94 (7.45%) patients died whereas 80 (85.1%) patients were discharged under stable conditions and 7 (7.45%) were discharged on request with stable vitals.

Table 24 - Incidence of different outcomes among the study group

Outcome	No. of cases	Percentage
DISCHARGE	80	85.1%
DOR	7	7.45%
DEATH	7	7.45%
Total	94	100.0%

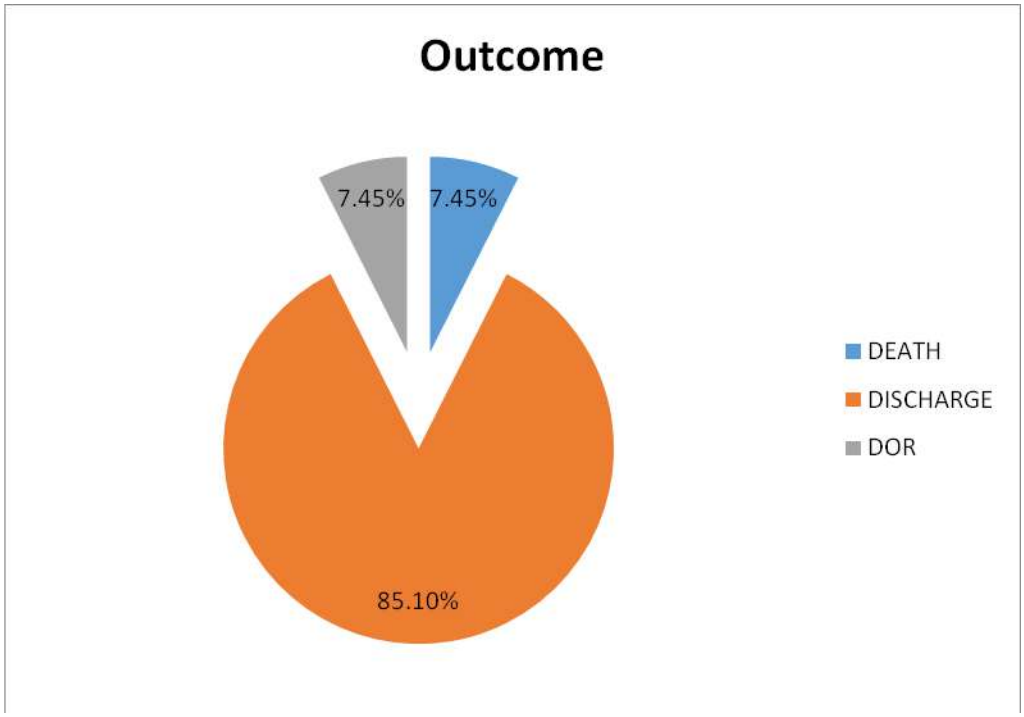

Fig 21 - Incidence of different outcomes among the study group

DISCUSSION

Acute pancreatitis is a common disease entity. The early identification of potentially severe acute pancreatitis enables the selection of patients who may require a more intensive and invasive method of management than is appropriate in mild pancreatitis and can play a significant role in management decisions and in reducing the morbidity and mortality associated with severe acute pancreatitis. Ranson's score, Glasgow score, APACHE II, Marshall, and SOFA (Sepsis-related organ failure assessment) scoring system are different severity scoring system studied in the past and proven to be indicators of the clinical severity. But, none of the above scoring systems are proven to be the precise indicators of the adverse clinical outcome. Our study expands the knowledge about early noninvasive predictors of severity and mortality in AP, namely RDW and RDW:TSC, which are easy to determine. Here is how our results compare to those of similar studies done in the past.

AGE-

The mean age of our study group is 43.32 years which is comparable to other studies on acute pancreatitis. As mentioned in table 23 and figure 23, we can observe the mean age comparison among different studies. Our study group's mean age (43.32 years) is comparable to Tao Peng et al study (48 years).[130]

Table 25: Mean Age in similar studies

Study	Mean age (years)
This study	43.32 years
Marta Gravito-Soares et al (2018)[105]	66.3 ± 15.1 years
Tao Peng et al (2017)[130]	48 years
Cetinkaya E et al (2014)[131]	56.5 years
Dong Wang et al (2015)[132]	51.2 ± 18.5 years
Robert M. O'Connell et al (2018)[133]	50.39 years

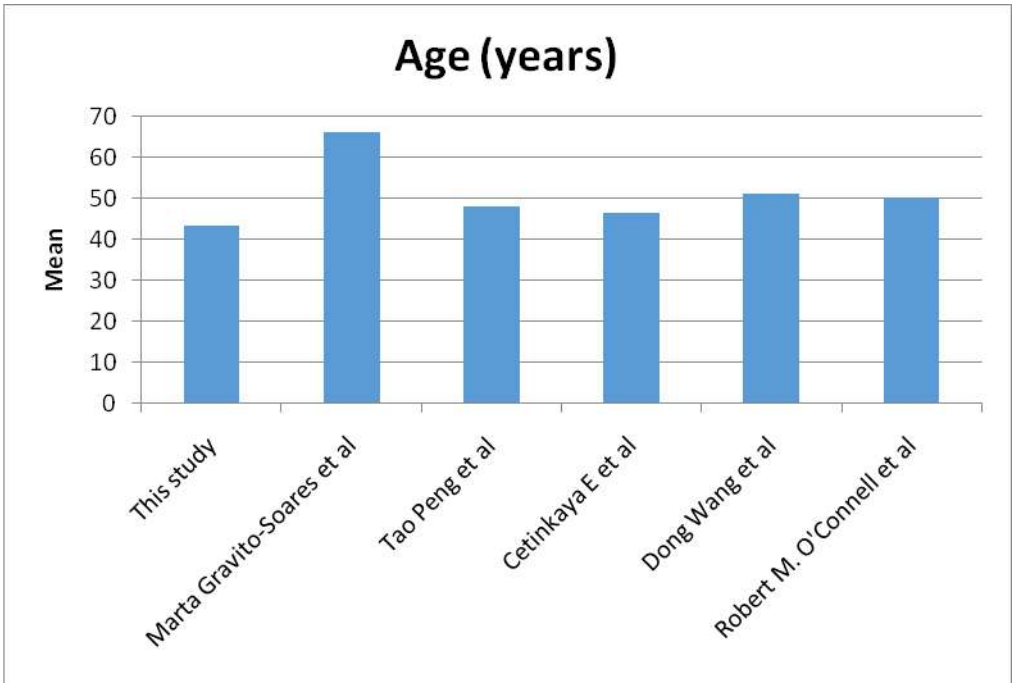

Fig 22: Mean Age in similar studies

SEX-

Our study showed a high predominance of male patients as opposed to females which is comparable to other studies. Our study group's gender distribution is comparable to Tao Peng et al study (2017).[130]

Table 26 - Gender distribution among different study groups

Study	Male (%)	Female (%)
This study	63.8 %	36.2 %
Marta Gravito-Soares et al (2018)[105]	54.9 %	45.1%
Tao Peng et al (2017)[130]	61.4 %	38.6%
Cetinkaya E et al (2014)[131]	57.8 %	42.2 %
Dong Wang et al (2015)[132]	41.7 %	58.3 %
Robert M. O'Connell et al (2018)[133]	53.5 %	46.5 %

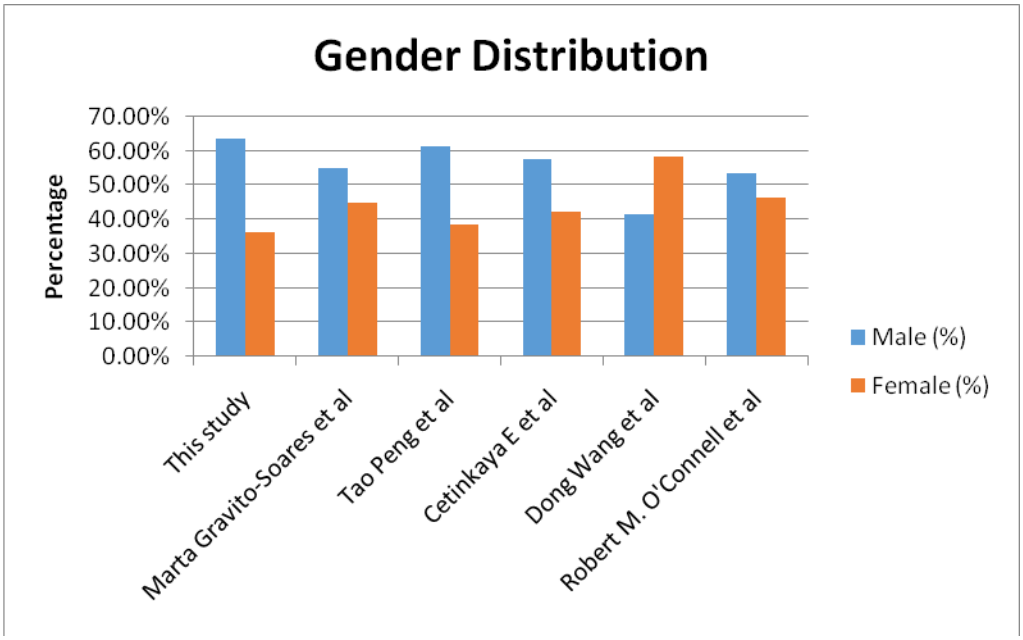

Fig 23 - Gender distribution among different study groups

ETIOLOGY-

In our study, the most common cause of acute pancreatitis was biliary (46.8 %) followed by alcohol (34.0%). This was comparable to Tao Peng et al study (2017).[130]

Table 27 - Distribution of acute pancreatitis on basis of etiology among different study groups

Study	Most common cause	2nd most common cause
This study	Biliary (46.8%)	Alcohol (34%)
Marta Gravito-Soares et al (2018)[105]	Biliary (56%)	Alcohol (19.55%)
Tao Peng et al (2017)[130]	Biliary (53.16%)	Alcohol (25.32%)
Cetinkaya E et al (2014)[131]	Biliary (73.5%)	Alcohol (36.27%)
Dong Wang et al (2015)[132]	Biliary (84.25%)	Alcohol (20.22%)

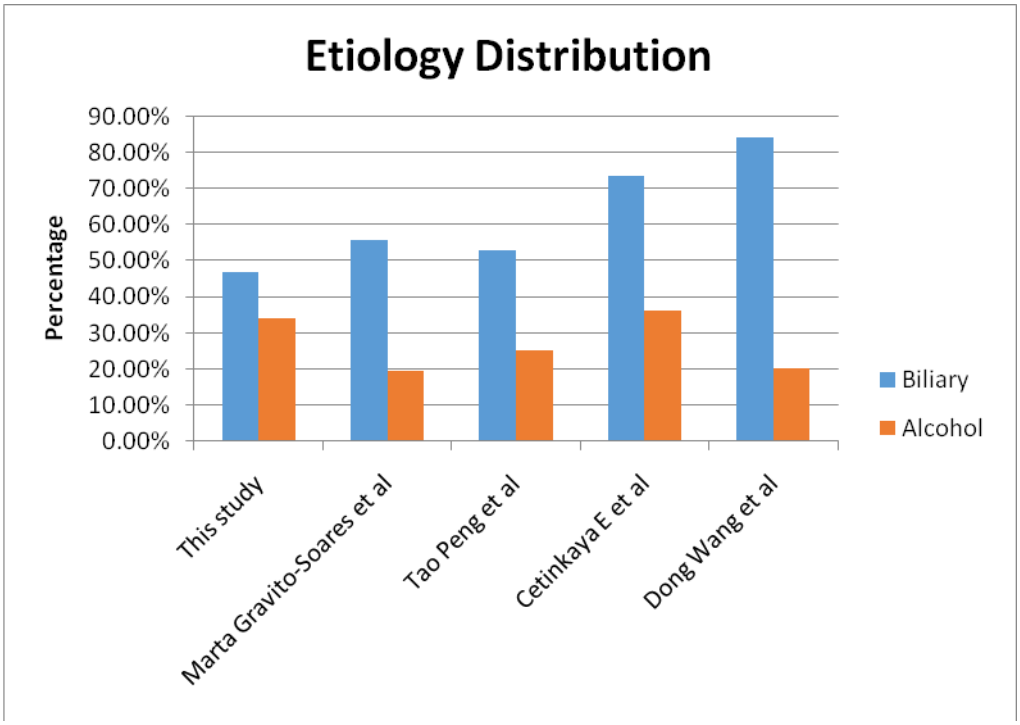

Fig 24 - Distribution of acute pancreatitis on basis of etiology among different study groups

ORGAN FAILURE-

In our study, 53.2% of patients had organ failure out of which 47.9% had respiratory failure. This is comparable to Marta Gravito-Soares et al study (2018)[105] where 46.2% of patients had organ failure with the most common being respiratory failure (33%)

Table 28 - Incidence of organ failure among different study groups

Study	Organ Failure (%)
This study	53.2%
Marta Gravito-Soares et al (2018)[105]	46.2%
Tao Peng et al (2017)[130]	25.05%
Dong Wang et al (2015)[132]	25.83%

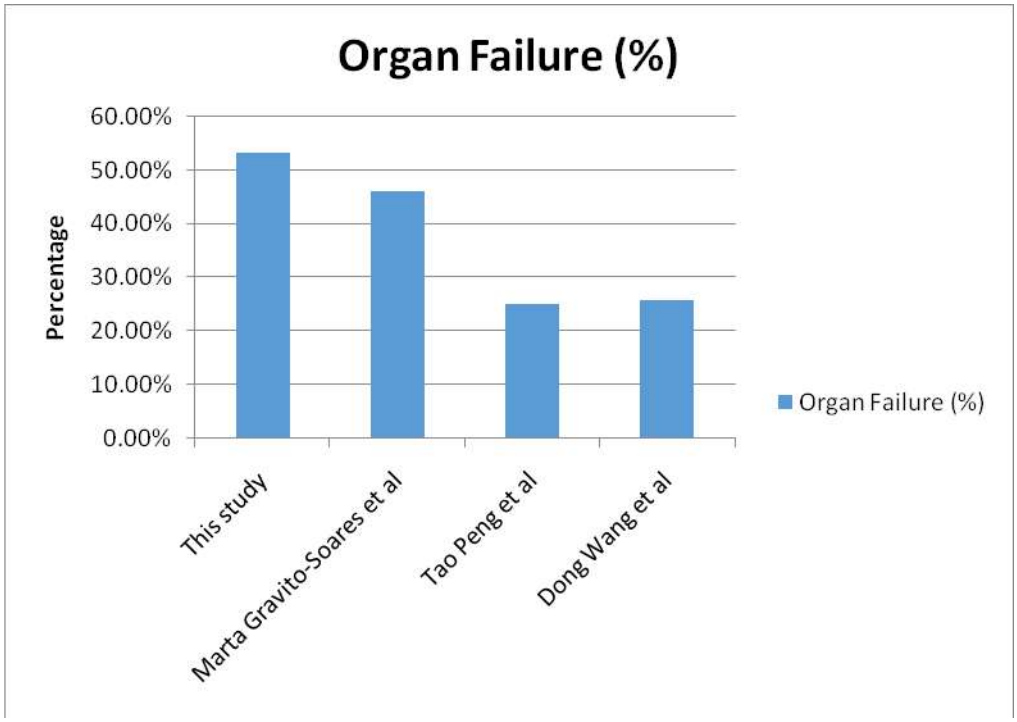

Figure 25 - Incidence of organ failure among different study groups

CORRELATION OF RDW TO SEVERITY OF ACUTE PANCREATITIS - In our study, RDW (AUROC:0.997; p - 0.000 i.e. significant) is a major predictor of severe AP to a cut-off value of 16.25% (S-100%; Sp-97.1%). This is comparable to Marta Gravito-Soares et al study (2018)[105] which concluded RDW0h (AUROC:0.960; p< 0.001) as a major predictor of severe AP to a cut-off value of 13.0% (S-92.7%; Sp-84.3%).

Table 29 - Correlation of RDW to the severity of acute pancreatitis among different study groups

Study	RDW cut off (%)
This study	16.25 %
Marta Gravito-Soares et al (2018)[105]	13 %
Tao Peng et al (2017)[130]	13.05 %

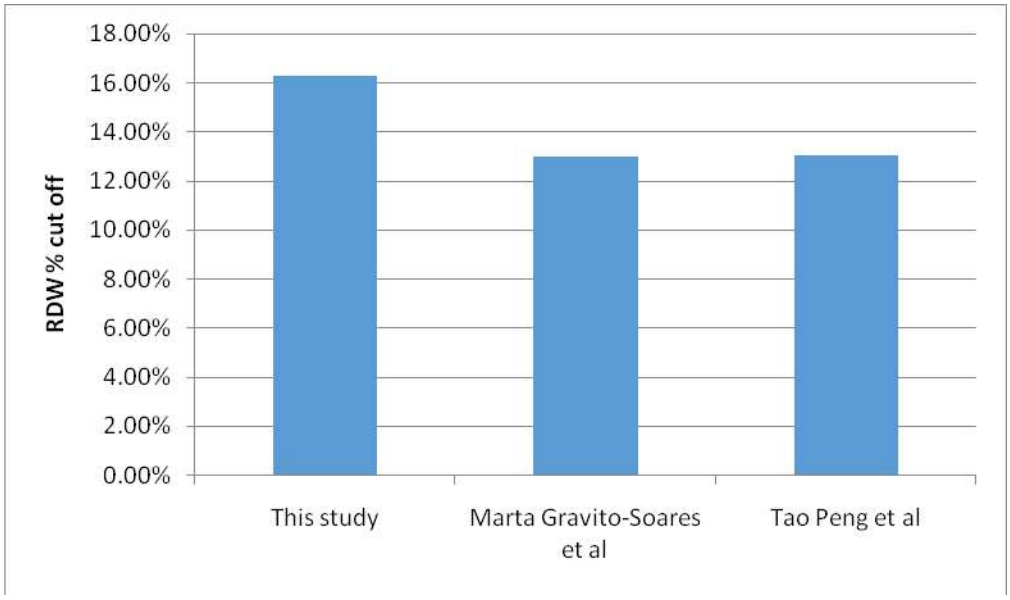

Figure 26 - Correlation of RDW to the severity of acute pancreatitis among different study groups

CORRELATION OF RDW:TSC TO SEVERITY OF ACUTE PANCREATITIS -

In our study, the RDW-to-TSC ratio (AUROC:1; p-0.000 i.e significant) is a major predictor of severe AP to a cut-off value of 2.42 (Senstivity-100%; Sp-100%). This is comparable to Marta Gravito-Soares et al study (2018)[105] which concluded RDW0h-to-TSC ratio (AUROC:0.973; p < 0.001) as a major predictor of severe AP to a cut-off value of 1.4 (S-96.3%; Sp-84.3%)

Table 30 - Correlation of RDW:TSC to the severity of acute pancreatitis among different study groups

Study	RDW:TSC cut off
This study	2.42
Marta Gravito-Soares et al (2018)[105]	1.4

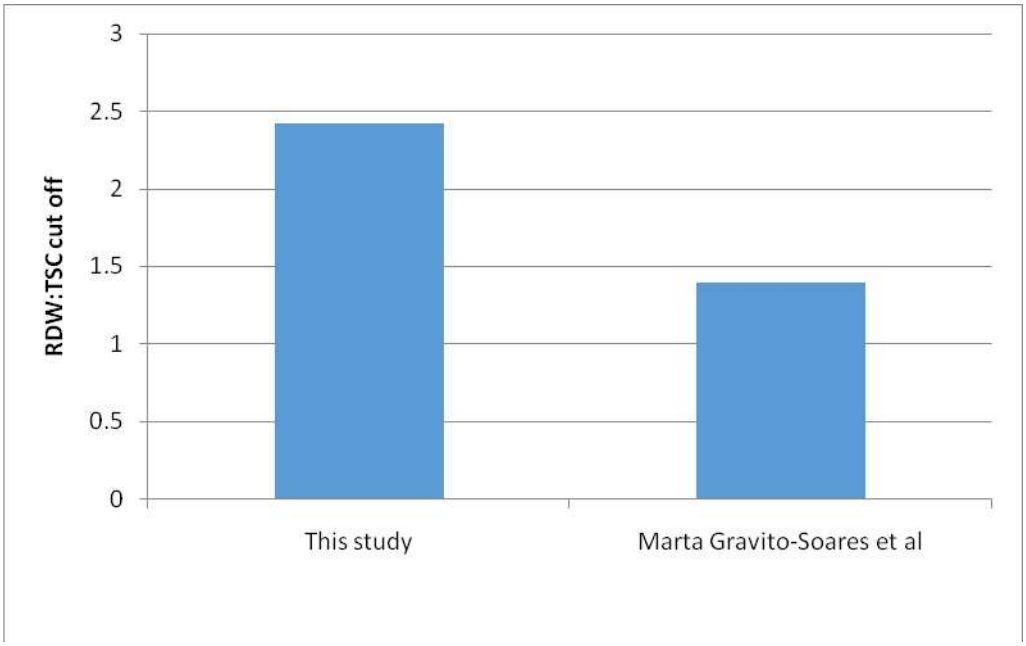

Figure 27- Correlation of RDW:TSC to the severity of acute pancreatitis among different study groups

CORRELATION OF RDW WITH MORTALITY IN ACUTE PANCREATITIS -

In our study, RDW(AUROC:0.947; p- 0.000 i.e significant) is a major predictor of mortality in AP to a cut-off value of 17.20% (S-100%; Sp-87.4%). This is comparable to Marta Gravito-Soares et al study (2018)[105] which concluded RDW (AUROC: 0.842; p < 0.001) as a major predictor of mortality in AP to a cut-off value of 14%.

Table 31 - Correlation of RDW with mortality in acute pancreatitis among different study groups

Study	RDW cut off (%)
This study	17.20 %
Marta Gravito-Soares et al (2018)[105]	14 %
Dong Wang et al (2015)[132]	14.35 %

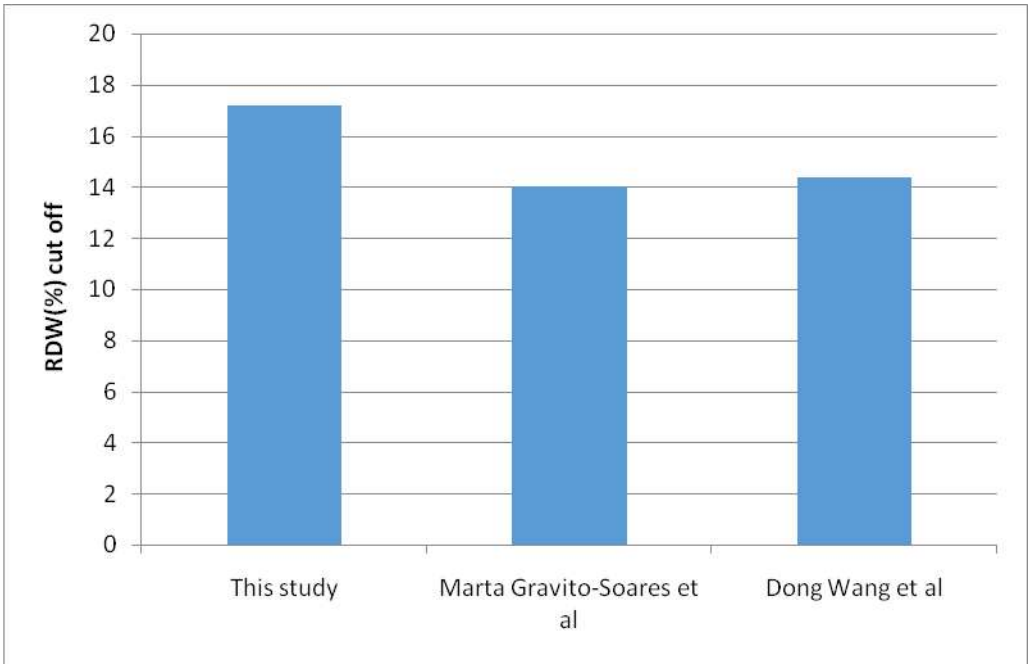

Figure 28 - Correlation of RDW with mortality in acute pancreatitis among different study groups

CORRELATION OF RDW:TSC WITH MORTALITY IN ACUTE PANCREATITIS -

In our study, the RDW-to-TSC ratio (AUROC:0.975; p-0.000) is a major predictor of mortality in AP to a cut-off value of 2.9 (Senstivity-100%; Sp-96.6%). This is comparable to Marta Gravito-Soares et al study (2018)[105] which concluded RDW (AUROC: 0.820; p < 0.001) as a major predictor of mortality in AP to a cut-off value of 14.

Table 32 - Correlation of RDW:TSC with mortality in acute pancreatitis among different study groups

Study	RDW:TSC cut off
This study	2.9
Marta Gravito-Soares et al (2018)[105]	1.7

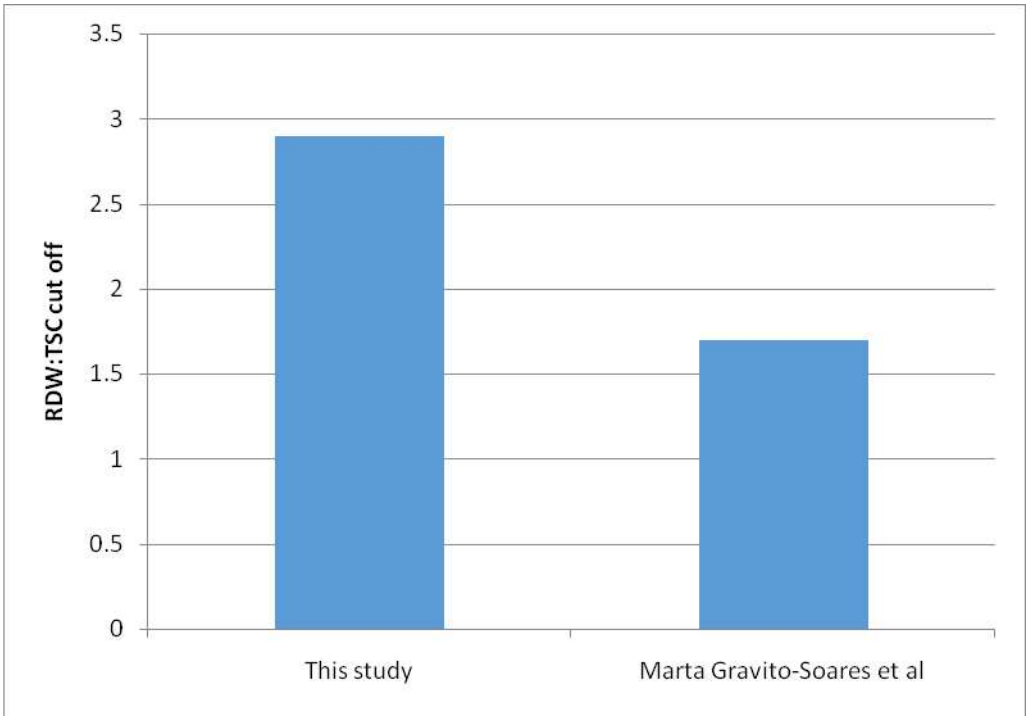

Figure 29 - Correlation of RDW:TSC with mortality in acute pancreatitis among different study groups

MORTALITY-

In our study, the mortality rate was observed to be 7.45% which is comparable to Marta Gravito-Soares et al study (2018)[105] and Tao Peng et al study (2017).[130]

Table 33- Mortality rate among different study groups

Study	Mortality Rate (%)
This study	7.45 %
Marta Gravito-Soares et al (2018)[105]	8.8%
Tao Peng et al (2017)[130]	8.23 %
Cetinkaya E et al (2014)[131]	12.74%
Dong Wang et al (2015)[132]	13.33%
Robert M. O'Connell et al (2018)[133]	1.08%

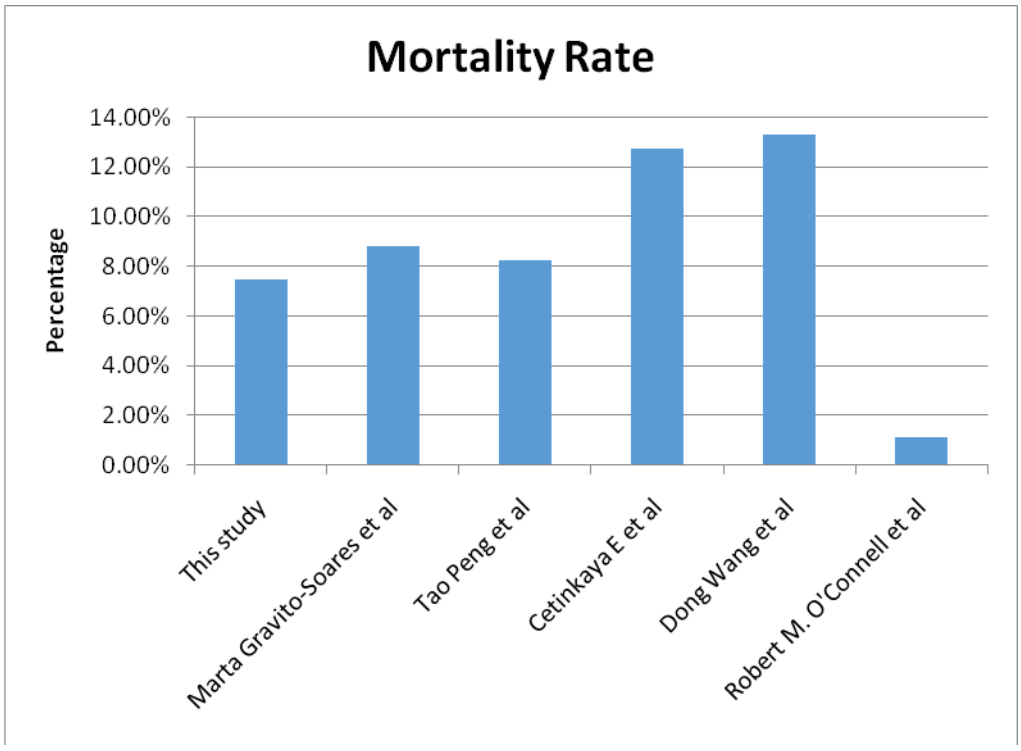

Figure 30- Mortality rate among different study groups

SUMMARY AND CONCLUSION

This prospective study was conducted on patients who were diagnosed as a case of acute pancreatitis admitted in Dayanand Medical College and Hospital, Ludhiana from 1st January, 2019 to 31st December, 2019. This study included 94 patients who fit in inclusion criteria. We aimed at evaluating the predictive power of RDW and RDW to TSC ratio in assessing severity and mortality in AP and providing a cut off value for both RDW and RDW to TSC ratio for severity and mortality in AP.

In this study, the Mean age observed was 43.32 years. Most of them belonged to the age group of 31-40 years (25.5%) followed by <30 years (24.5%). Most of the patients (63.8%) were males while 36.2% were females. The most common symptom in patients with acute pancreatitis was pain abdomen (98.9%) followed by vomiting (37.2%). The most common cause of acute pancreatitis was biliary (46.8 %) followed by alcohol (34.0%).

In this study, 53.2% patients had organ failure. 47.9% of patients had respiratory failure, 10.6% had renal failure and 4.3% had cardiovascular failure. 46.8% of patients had mild acute pancreatitis, 27.7% had moderately severe pancreatitis while 25.5% had severe pancreatitis.

Cut off for RDW (AUROC:0.997; p-0.000 i.e. significant) to predict severity of AP was 16.25%(Senstivity-100%; Specificity-97.1%) while that of RDW-to-TSC ratio (AUROC:1; p-0.000 i.e significant) was 2.42(Senstivity-100%; Specificity-100%). Both, RDW and RDW:TSC, were observed to be major predictors of severe AP. Similarly, cut off for RDW (AUROC:0.947; p-0.000 i.e significant) to predict mortality in AP was 17.20%(Senstivity-100%; Specificity-87.4%) and that of RDW-to-TSC ratio (AUROC:0.975; p-0.000 i.e significant) was 2.9(Senstivity-100%; Sp-96.6%).Both, RDW and RDW:TSC, were observed to be major predictors of mortality in AP.

In our study, 7.4% of patients required Per-cutaneous drainage of peripancreatic collection, 6.4% patients required pancreatic necrosectomy while only 1.1% patients required endoscopic nasocystic drainage. Mean RDW for patients requiring endoscopic nasocystic

drainage, pancreatic necrosectomy, and percutaneous drainage of peripancreatic collection was 14.20 %, 17.38±0.685%, and 17.59±2.335% respectively while RDW:TSC requiring nasocystic drainage, pancreatic necrosectomy and percutaneous drainage of peripancreatic collection were 2.21, 2.83±0.201 and 2.56±0.384 respectively. In our study, mortality rate was observed to be 7.45%.

However, few limitations were present in the study. The sample size of the study was small compared to other studies. RDW and Serum calcium samples were collected from a single center and thus, RDW:TSC levels could have been slightly different in other populations studied. Our study was done in a tertiary care center so varied treatments given in the 48 hours at primary centers affected the mortality, hence might not be correct to compare with other studies. Additionally, we have not directly compared RDW:TSC with established clinically used criteria, such as Ranson, APACHE-II, etc, because these parameters were not captured in the clinical database used in this study. Thus more large, multicenter and comparative cohort studies are needed.

In conclusion, our study found that RDW and RDW:TSC were good prognostic predictors of severity and death in AP patients. Increased RDW and RDW:TSC can be used as new indicators of mortality in patients with AP. These results indicate that RDW and RDW:TSC are convenient, economic, and sensitive monitoring methods for helping clinicians predict severity and death in AP patients.

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Sr no.	MRD No.	Name	Age	Sex	Hospital stay	Chief Complaints				Personal History			BLOOD PRESSURE (mmHg)	PULSE RATE (/min)
						Pain Abdomen	VOMITTING	FEVER	BREATHLESSNESS	ALCOHOL	SMOKING	DRUG ABUSE		
1	655679	MS	24	MALE	21	YES	NO	NO	NO	YES	NO	NO	110/70	88
2	660323	NS	55	FEMALE	10	YES	NO	NO	NO	NO	NO	NO	140/100	104
3	659637	BS	32	MALE	8	YES	NO	NO	NO	YES	NO	NO	150/70	80
4	670948	P	27	FEMALE	6	YES	NO	NO	NO	NO	NO	NO	110/70	80
5	676735	NS	32	MALE	22	YES	YES	NO	NO	YES	NO	NO	130/90	114
6	682905	GS	46	MALE	12	YES	YES	NO	YES	YES	NO	NO	120/80	128
7	685787	RW	65	FEMALE	33	YES	YES	NO	YES	NO	NO	NO	140/80	100
8	699438	U	35	FEMALE	7	YES	NO	NO	NO	NO	NO	NO	120/70	78
9	693383	GS	50	MALE	6	YES	NO	NO	NO	YES	NO	NO	120/80	88
10	702609	JS	58	MALE	18	YES	NO	NO	YES	NO	NO	NO	110/70	88
11	705939	MB	48	FEMALE	7	YES	YES	NO	NO	NO	NO	NO	110/70	86
12	546826	PL	28	FEMALE	6	YES	NO	NO	NO	NO	NO	NO	106/70	74
13	706197	AM	28	MALE	9	YES	NO	NO	NO	YES	NO	NO	90/60	88
14	711608	LS	42	MALE	13	YES	YES	NO	YES	YES	NO	NO	110/70	86
15	715552	KS	65	MALE	14	YES	NO	NO	NO	YES	NO	NO	140/90	114
16	715548	RK	68	MALE	12	YES	YES	NO	NO	YES	NO	NO	100/60	100
17	716201	NS	70	MALE	9	YES	YES	NO	NO	NO	NO	NO	120/70	86
18	717741	JS	50	MALE	14	YES	YES	NO	NO	YES	NO	NO	110/70	86
19	718631	JK	58	FEMALE	9	YES	YES	NO	YES	NO	NO	NO	160/90	118
20	724739	CP	67	FEMALE	8	YES	NO	YES	NO	NO	NO	NO	100/70	99
21	727967	MJ	40	MALE	5	YES	YES	NO	NO	NO	NO	NO	124/70	110
22	530707	DU	36	FEMALE	14	YES	NO	NO	YES	NO	NO	NO	120/70	82
23	749609	IS	60	MALE	18	YES	NO	NO	NO	YES	NO	NO	110/70	88
24	751259	SK	39	MALE	7	YES	YES	NO	NO	NO	NO	NO	110/70	86
25	752965	MS	35	MALE	14	YES	NO	NO	YES	YES	YES	NO	110/70	78
26	639391	SP	42	FEMALE	8	YES	NO	NO	NO	NO	NO	NO	120/70	72
27	752783	KK	37	FEMALE	8	YES	YES	YES	NO	NO	NO	NO	110/70	86

Sr no.	MRD No.	Name	Age	Sex	Hospital stay	Chief Complaints				Personal History			BLOOD PRESSURE (mmHg)	PULSE RATE (/min)
						Pain Abdomen	VOMITTING	FEVER	BREATHLESSNESS	ALCOHOL	SMOKING	DRUG ABUSE		
28	755273	KS	48	MALE	13	YES	YES	NO	NO	YES	NO	NO	110/70	92
29	209262	G	26	MALE	9	YES	NO	NO	NO	NO	NO	NO	110/66	86
30	758002	SK	42	FEMALE	18	YES	YES	NO	NO	NO	NO	NO	110/70	94
31	762621	JS	70	MALE	19	YES	NO	NO	YES	NO	NO	YES	120/80	88
32	771941	V	17	MALE	15	YES	YES	YES	NO	NO	NO	NO	100/60	106
33	775796	CB	40	MALE	45	YES	NO	NO	NO	YES	NO	NO	110/70	86
34	779092	SA	21	MALE	10	YES	NO	NO	NO	NO	NO	YES	114/70	90
35	782250	BS	38	MALE	19	YES	NO	NO	NO	YES	NO	NO	110/70	92
36	786070	JS	30	MALE	20	YES	NO	NO	NO	YES	NO	NO	120/70	96
37	786982	SK	27	MALE	15	YES	NO	NO	NO	NO	NO	NO	110/70	86
38	787885	RR	40	FEMALE	7	YES	NO	NO	NO	NO	NO	NO	130/80	82
39	795278	AG	24	MALE	26	YES	NO	NO	YES	YES	NO	NO	120/70	90
40	547936	SC	42	MALE	7	YES	NO	NO	NO	NO	NO	NO	100/60	90
41	800392	TS	76	MALE	14	YES	NO	NO	NO	NO	NO	NO	150/90	86
42	803049	KK	54	MALE	8	YES	YES	NO	NO	NO	NO	NO	120/70	84
43	811498	GS	74	MALE	12	YES	YES	NO	YES	NO	NO	NO	110/80	84
44	804305	PB	60	MALE	6	YES	NO	NO	NO	NO	NO	NO	110/70	90
45	813364	MK	52	FEMALE	42	YES	YES	NO	NO	NO	NO	NO	100/60	88
46	812284	AC	45	MALE	11	YES	YES	NO	NO	YES	NO	NO	120/72	100
47	402152	DS	56	MALE	5	YES	NO	NO	NO	YES	NO	NO	108/70	80
48	820983	KC	44	MALE	18	YES	NO	NO	YES	YES	NO	NO	110/66	88
49	816596	NL	37	MALE	12	YES	NO	NO	NO	NO	NO	NO	122/76	84
50	497410	CS	28	MALE	3	YES	YES	YES	YES	YES	YES	NO	100/60	98
51	822179	VS	37	MALE	8	YES	YES	NO	NO	YES	NO	NO	112/70	84
52	822079	MS	58	FEMALE	6	YES	YES	NO	NO	NO	NO	NO	110/72	100
53	828412	RS	35	FEMALE	42	YES	YES	NO	YES	NO	NO	NO	90/60	102
54	327577	ML	62	MALE	24	YES	YES	NO	NO	NO	NO	NO	140/90	94

Sr no.	MRD No.	Name	Age	Sex	Hospital stay	Chief Complaints				Personal History			BLOOD PRESSURE (mmHg)	PULSE RATE (/min)
						Pain Abdomen	VOMITTING	FEVER	BREATHLESSNESS	ALCOHOL	SMOKING	DRUG ABUSE		
55	823267	GS	44	MALE	20	YES	NO	YES	YES	YES	NO	NO	110/78	98
56	828904	AS	23	MALE	51	YES	YES	NO	YES	YES	NO	NO	90/60	116
57	834948	MS	53	MALE	8	YES	NO	NO	NO	NO	NO	NO	110/76	84
58	834957	SD	55	FEMALE	43	NO	YES	NO	NO	NO	NO	NO	110/70	82
59	811496	HS	18	MALE	5	YES	NO	NO	NO	NO	NO	NO	120/74	90
60	324778	SD	54	MALE	5	YES	YES	NO	YES	YES	NO	NO	80/40	112
61	836742	S	45	MALE	15	YES	NO	NO	NO	YES	NO	NO	130/90	90
62	845873	KK	27	MALE	4	YES	NO	NO	NO	NO	NO	NO	106/70	86
63	846481	GS	44	MALE	8	YES	NO	NO	NO	YES	NO	NO	110/68	80
64	848006	SK	36	FEMALE	16	YES	NO	NO	NO	NO	NO	NO	120/70	84
65	849469	MS	19	FEMALE	24	YES	NO	NO	NO	NO	NO	NO	100/60	110
66	851884	G	29	MALE	41	YES	NO	NO	YES	YES	NO	NO	120/70	80
67	857626	NJ	36	FEMALE	12	YES	NO	NO	NO	NO	NO	NO	130/90	110
68	858630	LS	34	MALE	2	YES	NO	NO	YES	YES	NO	NO	60	126
69	872065	MP	46	FEMALE	6	YES	NO	NO	NO	NO	NO	NO	110/64	80
70	863635	AS	62	MALE	11	YES	NO	NO	NO	YES	NO	NO	100/68	100
71	876617	SD	21	FEMALE	13	YES	YES	NO	NO	NO	NO	NO	94/60	110
72	883782	VB	38	MALE	22	YES	NO	NO	NO	NO	NO	NO	110/68	106
73	887494	AS	36	MALE	12	YES	NO	NO	NO	NO	NO	NO	110/70	108
74	888182	RK	37	MALE	15	YES	NO	NO	NO	NO	NO	NO	140/80	68
75	888770	RK	55	FEMALE	8	YES	NO	NO	NO	NO	NO	NO	90/60	100
76	888794	RR	35	FEMALE	10	YES	NO	NO	YES	NO	NO	NO	100/60	160
77	889346	GM	33	MALE	11	YES	NO	NO	NO	YES	YES	NO	120/70	106
78	890575	RK	60	MALE	17	YES	YES	NO	NO	YES	NO	NO	110/70	110
79	890018	SK	26	MALE	15	YES	NO	NO	NO	YES	NO	NO	132/82	102
80	891138	RD	36	FEMALE	4	YES	NO	NO	NO	NO	NO	NO	110/70	90
81	893388	JS	70	MALE	25	YES	NO	NO	NO	YES	NO	NO	112/60	86

Sr no.	MRD No.	Name	Age	Sex	Hospital stay	Chief Complaints				Personal History			BLOOD PRESSURE (mmHg)	PULSE RATE (/min)
						Pain Abdomen	VOMITTING	FEVER	BREATHLESSNESS	ALCOHOL	SMOKING	DRUG ABUSE		
82	894018	SS	60	MALE	17	YES	NO	NO	NO	YES	NO	NO	120/80	136
83	894145	RK	38	FEMALE	6	YES	NO	NO	NO	NO	NO	NO	150/100	90
84	894778	PC	30	FEMALE	13	YES	YES	NO	NO	NO	NO	NO	130/80	60
85	895682	MS	28	FEMALE	13	YES	YES	NO	NO	NO	NO	NO	120/78	74
86	611484	AD	41	MALE	9	YES	NO	NO	NO	NO	NO	NO	110/60	94
87	898533	GK	49	FEMALE	7	YES	YES	NO	NO	NO	NO	NO	110/70	90
88	899150	DM	58	FEMALE	8	YES	NO	NO	NO	NO	NO	NO	130/90	90
89	899153	KD	70	FEMALE	11	YES	NO	NO	NO	NO	NO	NO	110/70	84
90	899182	SK	60	FEMALE	23	YES	NO	NO	NO	NO	NO	NO	120/90	120
91	899859	VK	30	MALE	11	YES	YES	NO	NO	NO	NO	NO	120/74	100
92	907967	JK	70	FEMALE	11	YES	YES	NO	NO	NO	NO	NO	104/70	92
93	912904	NA	20	MALE	20	YES	YES	YES	NO	NO	NO	NO	120/70	84
94	920274	LU	27	FEMALE	4	YES	NO	NO	NO	NO	NO	NO	114/70	86

Sr no.	MRD No.	Name	RESPIRATORY RATE (/min)	TEMPERATURE (°F)	Etiology	TLC ($x10^3$/uL)	RDW (%)	Blood Urea (mg/dl)	Creatinine (mg/dl)	S. AMYLASE (U/L)	S. LIPASE (U/L)	Serum Calcium (mg/dl)	RDW:TSC	PLEURAL EFFUSION
1	655679	MS	22	97.5	ALCOHOL	12.7	17.4	54	1.35	895	1383	5.8	3	YES
2	660323	NS	24	97	BILIARY	6.4	16.2	14	0.68	108	204	7.7	2.1	NO
3	659637	BS	20	98	ALCOHOL	16.2	14.1	45	0.88	574	644	9.2	1.53	NO
4	670948	P	24	98	IDIOPATHIC	17	13.6	21	0.60	2182	4108	9.4	1.44	NO
5	676735	NS	26	99	ALCOHOL	25.5	16.1	51	1.10	103	141	7.4	2.17	YES
6	682905	GS	26	97	ALCOHOL	12.3	15	19	0.77	77	199	7.1	2.11	YES
7	685787	RW	28	99.8	BILIARY	17.3	17.4	77	1.51	680	485	5.8	3	YES
8	699438	U	20	99	BILIARY	8.7	13.3	7	0.68	96	42	8.7	1.6	NO
9	693383	GS	20	98	ALCOHOL	14.9	14	28	0.89	452	188	8.4	1.66	NO
10	702609	JS	16	98.6	BILIARY	23.4	14.7	35	0.90	60	51	7	2.1	YES
11	705939	MB	16	98	BILIARY	6.6	13.8	6	0.33	60	36	8.7	1.5	NO
12	546826	PL	16	99	BILIARY	8.4	12	10	0.57	349	407	8	1.5	NO
13	706197	AM	16	98.6	ALCOHOL	15.7	14.6	16	0.48	253	250	8	1.82	NO
14	711608	LS	28	97.5	ALCOHOL	12.1	14	42	1.46	221	824	6.8	2.05	YES
15	715552	KS	20	99	ALCOHOL	12.1	13	86	1.5	102	68	7.3	1.78	NO
16	715548	RK	20	99	ALCOHOL	11.8	18.8	144	4.6	1336	849	7.1	2.6	YES
17	716201	NS	18	98.6	BILIARY	18.1	13	59	1.25	1987	2988	7.2	1.8	NO
18	717741	JS	16	99	ALCOHOL	8.9	17.5	42	0.95	627	373	6.4	2.7	YES
19	718631	JK	26	98.6	BILIARY	20.6	12.9	31	0.66	292	128	7.4	1.74	NO
20	724739	CP	20	100	BILIARY	2.9	13.2	26	0.75	534	366	8.7	1.51	NO
21	727967	MJ	22	98.6	IDIOPATHIC	12.7	12.6	42	1.04	1478	3015	8.4	1.5	NO
22	530707	DU	26	98	BILIARY	12.2	15.2	17	1.01	982	785	7	2.17	YES
23	749609	IS	20	99	ALCOHOL	11.1	18	37	0.84	626	1035	7	2.57	YES
24	751259	SK	16	98	BILIARY	13.4	14.7	11	0.57	323	401	8.7	1.6	NO
25	752965	MS	26	99	ALCOHOL	11	14.4	26	0.78	670	482	7.1	2.02	NO
26	639391	SP	22	98.4	POST ERCP	10.1	13	24	0.95	652	298	7.8	1.66	NO
27	752783	KK	16	99	POST ERCP	15.2	14	31	0.48	292	484	7.5	1.8	NO

Sr no.	MRD No.	Name	RESPIRATORY RATE (/min)	TEMPERATURE (°F)	Etiology	TLC ($x10^3$/uL)	RDW (%)	Blood Urea (mg/dl)	Creatinine (mg/dl)	S. AMYLASE (U/L)	S. LIPASE (U/L)	Serum Calcium (mg/dl)	RDW:TSC	PLEURAL EFFUSION
28	755273	KS	22	99	ALCOHOL	9.7	15	48	0.79	290	369	6.4	2.34	YES
29	209262	G	24	99.4	BILIARY	18.1	13	18	0.89	2117	4848	7.8	1.66	NO
30	758002	SK	24	99.5	BILIARY	23	16.4	11	0.6	253	482	4.4	3.7	YES
31	762621	JS	22	99	DRUG	22.1	14.2	100	4.04	670	913	6.4	2.21	YES
32	771941	V	22	99.5	BILIARY	14.5	16.7	24	0.7	180	240	8.1	2.01	YES
33	775796	CB	22	99.2	ALCOHOL	13.4	18.6	23	0.92	1223	1964	7	2.65	YES
34	779092	SA	24	98.7	DRUG	13.2	15.1	26	1.1	1345	874	9.6	1.57	YES
35	782250	BS	22	97.5	ALCOHOL	11.1	15	18	0.91	171	77	6.5	2.3	YES
36	786070	JS	24	96	ALCOHOL	18	21.5	36	0.64	41	43	7.6	2.8	NO
37	786982	SK	22	97	IDIOPATHIC	13	16.2	34	0.73	53	39	7.7	2.1	YES
38	787885	RR	22	98.4	BILIARY	7.8	12.4	23	0.67	328	429	8	1.55	NO
39	795278	AG	22	96.4	ALCOHOL	12.8	17.9	43	1.18	301	651	7	2.55	YES
40	547936	SC	22	99.2	IDIOPATHIC	8.3	13.3	20	1.08	210	183	9.7	1.3	NO
41	800392	TS	22	96.8	IDIOPATHIC	10.6	16.5	33	1.27	241	177	8	2.06	YES
42	803049	KK	20	98.8	BILIARY	15.5	15.2	34	0.97	208	127	6.4	2.3	YES
43	811498	GS	24	98	IDIOPATHIC	13.2	15.4	20	1.2	989	752	7.1	2.16	YES
44	804305	PB	22	98.6	IDIOPATHIC	12.4	14.5	23	0.74	247	555	8.6	1.68	YES
45	813364	MK	26	98.8	BILIARY	17	18.3	77	2.01	1960	2815	6.1	3	YES
46	812284	AC	24	98.2	ALCOHOL	9.1	14.7	21	0.39	327	1005	9.2	1.59	YES
47	402152	DS	20	96.2	ALCOHOL	17.4	13.8	33	1.01	181	180	8.8	1.56	YES
48	820983	KC	26	98.4	ALCOHOL	12	14.8	54	2.1	2181	1468	7.4	2	YES
49	816596	NL	24	98	BILIARY	7.1	13.4	17	0.77	524	1041	9	1.48	NO
50	497410	CS	28	101	ALCOHOL	14	18.4	64	1.41	1900	1650	5.9	3.11	YES
51	822179	VS	24	96.8	BILIARY	11	12.2	31	0.77	206	250	7.7	1.58	YES
52	822079	MS	24	98.8	BILIARY	14.5	13	19	0.6	804	1044	8.9	1.46	NO
53	828412	RS	28	99.4	BILIARY	15	17.8	40	1.1	2146	1784	6.1	2.91	YES
54	327577	ML	24	99.1	BILIARY	20.3	17.6	45	1.1	2113	2911	6.3	2.79	NO

Sr no.	MRD No.	Name	RESPIRATORY RATE (/min)	TEMPERATURE (°F)	Etiology	TLC ($x10^3$/uL)	RDW (%)	Blood Urea (mg/dl)	Creatinine (mg/dl)	S. AMYLASE (U/L)	S. LIPASE (U/L)	Serum Calcium (mg/dl)	RDW:TSC	PLEURAL EFFUSION
55	823267	GS	32	100	ALCOHOL	18.1	18	17	1.5	1556	1483	5.9	3.05	YES
56	828904	AS	30	99	ALCOHOL	14.3	17	77	1.71	1156	1340	5.9	2.88	YES
57	834948	MS	22	98	BILIARY	12.4	13	33	0.85	1793	2301	9	1.44	YES
58	834957	SD	18	98	POST ERCP	13.7	17.5	51	1.79	1675	1831	7	2.5	YES
59	811496	HS	24	99.6	BILIARY	4.7	13.2	13	0.76	204	559	8.5	1.55	NO
60	324778	SD	32	100	ALCOHOL	11.4	18	54	2.55	1254	1600	6	3	YES
61	836742	S	18	98	ALCOHOL	19	16	33	1.01	804	1227	7.9	2.02	NO
62	845873	KK	26	97	AUTOIMMUNE	12.4	14.2	27	0.75	755	2113	8.6	1.65	NO
63	846481	GS	24	97.1	ALCOHOL	16.8	13.8	21	0.8	882	1331	8.7	1.58	NO
64	848006	SK	22	99	BILIARY	19	15.8	23	0.55	2308	2691	7.2	2.19	NO
65	849469	MS	26	101	BILIARY	11.4	15.9	12	0.37	564	433	6.9	2.3	NO
66	851884	G	26	98	ALCOHOL	13.7	16.3	91	2	592	2517	6.1	2.67	NO
67	857626	NJ	24	99.4	IDIOPATHIC	6.9	15.6	70	1.24	2187	1981	7	2.22	NO
68	858630	LS	26	101	ALCOHOL	19.9	20.1	88	3.5	4941	6345	6.1	3.29	YES
69	872065	MP	24	98	BILIARY	8.4	12.8	18	0.74	438	597	7.7	1.66	NO
70	863635	AS	22	96.6	BILIARY	12.2	18.2	17	0.97	46	82	6.5	2.8	YES
71	876617	SD	24	99.6	BILIARY	20.2	14.3	15	0.42	264	230	7.9	1.8	NO
72	883782	VB	20	98.6	BILIARY	12.8	13	8	0.74	1965	5089	7.4	1.75	NO
73	887494	AS	24	100.6	BILIARY	18.7	12.5	26	0.87	92	95	8	1.56	YES
74	888182	RK	24	98	BILIARY	17.4	17	22	0.93	1290	1714	6	2.8	YES
75	888770	RK	24	100	BILIARY	24.3	13.3	40	0.44	342	262	7.5	1.77	NO
76	888794	RR	26	99.2	BILIARY	23.7	13.1	61	1.54	68	82	7.8	1.67	YES
77	889346	GM	24	98.6	ALCOHOL	21.8	12.8	19	0.84	37	35	8.7	1.4	YES
78	890575	RK	24	96	ALCOHOL	8.1	17	27	0.69	1212	981	5.3	3.2	YES
79	890018	SK	22	99	TRAUMA	13.5	15	34	0.99	58	319	7	2.1	YES
80	891138	RD	24	98.2	BILIARY	8.7	13	31	0.56	726	474	8	1.6	NO
81	893388	JS	26	99.3	ALCOHOL	15.5	16.5	105	4.3	560	468	6	2.75	YES

Sr no.	MRD No.	Name	RESPIRATORY RATE (/min)	TEMPERATURE (°F)	Etiology	TLC ($x10^3$/uL)	RDW (%)	Blood Urea (mg/dl)	Creatinine (mg/dl)	S. AMYLASE (U/L)	S. LIPASE (U/L)	Serum Calcium (mg/dl)	RDW:TSC	PLEURAL EFFUSION
82	894018	SS	24	97	ALCOHOL	18.4	16.1	42	1.18	1859	3265	8	2.01	YES
83	894145	RK	20	100.2	IDIOPATHIC	21	13.4	24	0.57	87	116	8.1	1.65	NO
84	894778	PC	24	98.2	BILIARY	6.4	13	14	0.56	1467	3553	8.7	1.49	YES
85	895682	MS	20	99	BILIARY	17.3	12.8	16	0.46	3060	2624	8.2	1.56	NO
86	611484	AD	24	97.8	BILIARY	14.8	13.2	15	0.79	132	74	7.8	1.69	YES
87	898533	GK	24	100.1	BILIARY	10.2	13.3	20	0.76	42	24	8.7	1.52	NO
88	899150	DM	20	98.4	BILIARY	14.2	13.7	44	0.65	600	640	8.8	1.55	NO
89	899153	KD	20	98.2	BILIARY	12.3	15.7	46	2	3610	1107	7.5	2.1	YES
90	899182	SK	24	99	BILIARY	17.8	17.4	78	2.69	1186	1130	6.1	2.85	YES
91	899859	VK	22	98.2	IDIOPATHIC	15.7	16	17	0.64	1370	763	8	2	YES
92	907967	JK	18	97	BILIARY	13.9	15.8	29	0.77	318	440	7.5	2.1	NO
93	912904	NA	20	101	BILIARY	14.1	16.2	34	0.84	145	91	7.7	2.1	NO
94	920274	LU	20	98.8	IDIOPATHIC	10.1	12.3	23	0.81	580	360	8	1.53	NO

Sr no.	MRD No.	Name	USG ABDOMEN	PANCREATIC NECROSIS CT/MRI	PaO2:FiO2	Organ Failure			Type of Organ Failure	Type of Pancreatitis	Intervention	Outcome
						Respiratory	Renal	Cardiovascular				
1	655679	MS	ACUTE PANCREATITIS	YES	246	YES	NO	NO	PERSISTENT	SEVERE	NO	DOR
2	660323	NS	ACUTE PANCREATITIS	NO	279	YES	NO	NO	TRANSIENT	MODERATELY SEVERE	NO	DISCHARGE
3	659637	BS	ACUTE PANCREATITIS	NO	391	NO	NO	NO	NO	MILD	NO	DISCHARGE
4	670948	P	ACUTE PANCREATITIS	YES	373	NO	NO	NO	NO	MILD	NO	DISCHARGE
5	676735	NS	ACUTE PANCREATITIS	YES	246	YES	NO	NO	TRANSIENT	MODERATELY SEVERE	NO	DOR
6	682905	GS	ACUTE PANCREATITIS	YES	246	YES	NO	NO	TRANSIENT	MODERATELY SEVERE	NO	DOR
7	685787	RW	ACUTE PANCREATITIS	YES	193	YES	NO	NO	PERSISTENT	SEVERE	YES (NECROSECTOMY)	DEATH
8	699438	U	ACUTE PANCREATITIS	NO	393	NO	NO	NO	NO	MILD	NO	DISCHARGE
9	693383	GS	ACUTE PANCREATITIS	NO	391	NO	NO	NO	NO	MILD	NO	DISCHARGE
10	702609	JS	ACUTE PANCREATITIS	NO	293	YES	NO	NO	TRANSIENT	MODERATELY SEVERE	YES (PCD)	DISCHARGE
11	705939	MB	ACUTE PANCREATITIS	NO	343	NO	NO	NO	NO	MILD	NO	DISCHARGE
12	546826	PL	ACUTE PANCREATITIS	NO	382	NO	NO	NO	NO	MILD	NO	DISCHARGE
13	706197	AM	ACUTE PANCREATITIS	NO	320	NO	NO	NO	NO	MILD	NO	DISCHARGE
14	711608	LS	ACUTE PANCREATITIS	NO	293	YES	NO	NO	TRANSIENT	MODERATELY SEVERE	NO	DISCHARGE
15	715552	KS	ACUTE PANCREATITIS	YES	382	NO	NO	NO	NO	MILD	NO	DOR
16	715548	RK	ACUTE PANCREATITIS	NO	206	YES	YES	NO	PERSISTENT	SEVERE	NO	DISCHARGE
17	716201	NS	ACUTE PANCREATITIS	NO	391	NO	NO	NO	NO	MILD	NO	DISCHARGE
18	717741	JS	ACUTE PANCREATITIS	YES	273	YES	NO	NO	PERSISTENT	SEVERE	NO	DISCHARGE
19	718631	JK	ACUTE PANCREATITIS	NO	346	NO	NO	NO	NO	MILD	NO	DISCHARGE
20	724739	CP	ACUTE PANCREATITIS	NO	352	NO	NO	NO	NO	MILD	NO	DISCHARGE
21	727967	MJ	ACUTE PANCREATITIS	NO	352	NO	NO	NO	NO	MILD	NO	DISCHARGE
22	530707	DU	ACUTE PANCREATITIS	NO	226	YES	NO	NO	TRANSIENT	MODERATELY SEVERE	NO	DISCHARGE
23	749609	IS	ACUTE PANCREATITIS	YES	246	YES	NO	NO	PERSISTENT	SEVERE	NO	DISCHARGE
24	751259	SK	ACUTE PANCREATITIS	NO	391	NO	NO	NO	NO	MILD	NO	DISCHARGE
25	752965	MS	ACUTE PANCREATITIS	NO	258	YES	NO	NO	TRANSIENT	MODERATELY SEVERE	NO	DOR
26	639391	SP	ACUTE PANCREATITIS	NO	348	NO	NO	NO	NO	MILD	NO	DISCHARGE
27	752783	KK	ACUTE PANCREATITIS	NO	343	NO	NO	NO	NO	MILD	NO	DISCHARGE

Sr no.	MRD No.	Name	USG ABDOMEN	PANCREATIC NECROSIS CT/MRI	PaO2:FiO2	Organ Failure			Type of Organ Failure	Type of Pancreatitis	Intervention	Outcome
						Respiratory	Renal	Cardiovascular				
28	755273	KS	ACUTE PANCREATITIS	NO	246	YES	NO	NO	TRANSIENT	MODERATELY SEVERE	NO	DISCHARGE
29	209262	G	ACUTE PANCREATITIS	NO	447	NO	NO	NO	NO	MILD	NO	DISCHARGE
30	758002	SK	ACUTE PANCREATITIS	NO	186	YES	NO	NO	PERSISTENT	SEVERE	NO	DISCHARGE
31	762621	JS	ACUTE PANCREATITIS	NO	193	YES	YES	NO	TRANSIENT	MODERATELY SEVERE	YES (NASOCYTIC DRAINAGE)	DISCHARGE
32	771941	V	ACUTE PANCREATITIS	NO	313	NO	NO	YES	TRANSIENT	MODERATELY SEVERE	NO	DISCHARGE
33	775796	CB	ACUTE PANCREATITIS	YES	193	YES	NO	NO	PERSISTENT	SEVERE	YES (PCD)	DISCHARGE
34	779092	SA	ACUTE PANCREATITIS	NO	313	NO	NO	NO	NO	MILD	NO	DISCHARGE
35	782250	BS	ACUTE PANCREATITIS	NO	206	YES	NO	NO	TRANSIENT	MODERATELY SEVERE	NO	DISCHARGE
36	786070	JS	ACUTE PANCREATITIS	YES	193	YES	NO	NO	PERSISTENT	SEVERE	YES (PCD)	DOR
37	786982	SK	ACUTE PANCREATITIS	NO	226	YES	NO	NO	TRANSIENT	MODERATELY SEVERE	NO	DISCHARGE
38	787885	RR	ACUTE PANCREATITIS	NO	410	NO	NO	NO	NO	MILD	NO	DISCHARGE
39	795278	AG	ACUTE PANCREATITIS	YES	273	YES	NO	NO	PERSISTENT	SEVERE	YES (PCD)	DISCHARGE
40	547936	SC	ACUTE PANCREATITIS	NO	391	NO	NO	NO	NO	MILD	NO	DISCHARGE
41	800392	TS	ACUTE PANCREATITIS	NO	293	YES	NO	NO	TRANSIENT	MODERATELY SEVERE	NO	DISCHARGE
42	803049	KK	ACUTE PANCREATITIS	YES	273	YES	NO	NO	TRANSIENT	MODERATELY SEVERE	NO	DISCHARGE
43	811498	GS	ACUTE PANCREATITIS	NO	298	YES	NO	NO	TRANSIENT	MODERATELY SEVERE	NO	DISCHARGE
44	804305	PB	ACUTE PANCREATITIS	NO	382	NO	NO	NO	NO	MILD	NO	DISCHARGE
45	813364	MK	ACUTE PANCREATITIS	YES	298	YES	YES	NO	PERSISTENT	SEVERE	YES (NECROSECTOMY)	DEATH
46	812284	AC	ACUTE PANCREATITIS	NO	408	NO	NO	NO	NO	MILD	NO	DISCHARGE
47	402152	DS	ACUTE PANCREATITIS	NO	400	NO	NO	NO	NO	MILD	NO	DISCHARGE
48	820983	KC	ACUTE PANCREATITIS	NO	321	NO	YES	NO	TRANSIENT	MODERATELY SEVERE	YES (PCD)	DISCHARGE
49	816596	NL	ACUTE PANCREATITIS	NO	391	NO	NO	NO	NO	MILD	NO	DISCHARGE
50	497410	CS	ACUTE PANCREATITIS	YES	220	YES	NO	NO	PERSISTENT	SEVERE	NO	DEATH
51	822179	VS	ACUTE PANCREATITIS	NO	300	NO	NO	NO	NO	MILD	NO	DISCHARGE
52	822079	MS	ACUTE PANCREATITIS	NO	417	NO	NO	NO	NO	MILD	NO	DISCHARGE
53	828412	RS	ACUTE PANCREATITIS	YES	215	YES	NO	NO	PERSISTENT	SEVERE	YES (NECROSECTOMY)	DEATH
54	327577	ML	ACUTE PANCREATITIS	YES	230	YES	NO	NO	PERSISTENT	SEVERE	YES (PCD)	DISCHARGE

Sr no.	MRD No.	Name	USG ABDOMEN	PANCREATIC NECROSIS CT/MRI	PaO2:FiO2	Organ Failure			Type of Organ Failure	Type of Pancreatitis	Intervention	Outcome
						Respiratory	Renal	Cardiovascular				
55	823267	GS	ACUTE PANCREATITIS	YES	228	YES	NO	NO	PERSISTENT	SEVERE	YES (PCD)	DEATH
56	828904	AS	ACUTE PANCREATITIS	YES	230	YES	NO	NO	PERSISTENT	SEVERE	YES (NECROSECTOMY)	DISCHARGE
57	834948	MS	ACUTE PANCREATITIS	NO	426	NO	NO	NO	NO	MILD	NO	DISCHARGE
58	834957	SD	ACUTE PANCREATITIS	YES	296	YES	NO	YES	PERSISTENT	SEVERE	YES (NECROSECTOMY)	DISCHARGE
59	811496	HS	ACUTE PANCREATITIS	NO	466	NO	NO	NO	NO	MILD	NO	DISCHARGE
60	324778	SD	ACUTE PANCREATITIS	YES	198	YES	YES	YES	PERSISTENT	SEVERE	NO	DEATH
61	836742	S	ACUTE PANCREATITIS	YES	243	YES	NO	NO	TRANSIENT	MODERATELY SEVERE	NO	DISCHARGE
62	845873	KK	ACUTE PANCREATITIS	NO	428	NO	NO	NO	NO	MILD	NO	DISCHARGE
63	846481	GS	ACUTE PANCREATITIS	NO	438	NO	NO	NO	NO	MILD	NO	DISCHARGE
64	848006	SK	ACUTE PANCREATITIS	YES	295	YES	NO	NO	TRANSIENT	MODERATELY SEVERE	NO	DISCHARGE
65	849469	MS	ACUTE PANCREATITIS	YES	260	YES	NO	NO	TRANSIENT	MODERATELY SEVERE	NO	DISCHARGE
66	851884	G	ACUTE PANCREATITIS	YES	400	NO	YES	NO	PERSISTENT	SEVERE	YES (NECROSECTOMY)	DISCHARGE
67	857626	NJ	ACUTE PANCREATITIS	NO	260	YES	NO	NO	TRANSIENT	MODERATELY SEVERE	NO	DISCHARGE
68	858630	LS	ACUTE PANCREATITIS	NO	180	YES	YES	YES	PERSISTENT	SEVERE	NO	DEATH
69	872065	MP	ACUTE PANCREATITIS	NO	418	NO	NO	NO	NO	MILD	NO	DISCHARGE
70	863635	AS	ACUTE PANCREATITIS	YES	260	YES	NO	NO	PERSISTENT	SEVERE	NO	DISCHARGE
71	876617	SD	ACUTE PANCREATITIS	NO	306	NO	NO	NO	NO	MILD	NO	DISCHARGE
72	883782	VB	ACUTE PANCREATITIS	NO	461	NO	NO	NO	NO	MILD	NO	DISCHARGE
73	887494	AS	ACUTE PANCREATITIS	NO	346	NO	NO	NO	NO	MILD	NO	DISCHARGE
74	888182	RK	ACUTE PANCREATITIS	YES	226	YES	NO	NO	PERSISTENT	SEVERE	NO	DISCHARGE
75	888770	RK	ACUTE PANCREATITIS	NO	540	NO	NO	NO	NO	MILD	NO	DISCHARGE
76	888794	RR	ACUTE PANCREATITIS	NO	360	NO	NO	NO	NO	MILD	NO	DISCHARGE
77	889346	GM	ACUTE PANCREATITIS	NO	306	NO	NO	NO	NO	MILD	NO	DISCHARGE
78	890575	RK	ACUTE PANCREATITIS	YES	270	YES	NO	NO	PERSISTENT	SEVERE	NO	DISCHARGE
79	890018	SK	ACUTE PANCREATITIS	NO	260	YES	NO	NO	TRANSIENT	MODERATELY SEVERE	NO	DOR
80	891138	RD	ACUTE PANCREATITIS	NO	408	NO	NO	NO	NO	MILD	NO	DISCHARGE
81	893388	JS	ACUTE PANCREATITIS	NO	295	YES	YES	NO	PERSISTENT	SEVERE	NO	DISCHARGE

Sr no.	MRD No.	Name	USG ABDOMEN	PANCREATIC NECROSIS CT/MRI	PaO2:FiO2	Organ Failure			Type of Organ Failure	Type of Pancreatitis	Intervention	Outcome
						Respiratory	Renal	Cardiovascular				
82	894018	SS	ACUTE PANCREATITIS	NO	290	YES	NO	NO	TRANSIENT	MODERATELY SEVERE	NO	DISCHARGE
83	894145	RK	ACUTE PANCREATITIS	NO	323	NO	NO	NO	NO	MILD	NO	DISCHARGE
84	894778	PC	ACUTE PANCREATITIS	NO	304	NO	NO	NO	NO	MILD	NO	DISCHARGE
85	895682	MS	ACUTE PANCREATITIS	NO	391	NO	NO	NO	NO	MILD	NO	DISCHARGE
86	611484	AD	ACUTE PANCREATITIS	NO	382	NO	NO	NO	NO	MILD	NO	DISCHARGE
87	898533	GK	ACUTE PANCREATITIS	NO	373	NO	NO	NO	NO	MILD	NO	DISCHARGE
88	899150	DM	ACUTE PANCREATITIS	NO	369	NO	NO	NO	NO	MILD	NO	DISCHARGE
89	899153	KD	ACUTE PANCREATITIS	NO	419	NO	YES	NO	TRANSIENT	MODERATELY SEVERE	NO	DISCHARGE
90	899182	SK	ACUTE PANCREATITIS	NO	361	NO	YES	NO	PERSISTENT	SEVERE	NO	DISCHARGE
91	899859	VK	ACUTE PANCREATITIS	NO	243	YES	NO	NO	TRANSIENT	MODERATELY SEVERE	NO	DISCHARGE
92	907967	JK	ACUTE PANCREATITIS	NO	233	YES	NO	NO	TRANSIENT	MODERATELY SEVERE	NO	DISCHARGE
93	912904	NA	ACUTE PANCREATITIS	YES	246	YES	NO	NO	TRANSIENT	MODERATELY SEVERE	NO	DISCHARGE
94	920274	LU	ACUTE PANCREATITIS	NO	461	NO	NO	NO	NO	MILD	NO	DISCHARGE

Baba Farid University
of Health Sciences
Sadiq Road
Faridkot-151 203 (Pb). INDIA.
Phone : 01639-256232,256236
Tele/Fax : 01639-256235
Email – Examination@bfuhs.ac.in

No. BFUHS/2K19p-TH/ 10432 Date 9/5/19

The Principal,
DMC, Ludhiana.

Subject: **Approval of Plan of Thesis.**

This is to inform you that the Faculty of Medical Sciences in its meeting held on 29.05.2019 has approved the plan of thesis of **Savjot Singh Narang**, a student of your college for **MS General Surgery** along with the names of Supervisor/Co-Supervisor as under:-

Topic Plan of Thesis

Red cell distribution width and ratio of red cell distribution width to serum calcium as predictors of outcome of acute pancreatitis

Supervisor
Dr. Chiranjiv Singh Gill
Prof.,
Dept. of Surgery,
DMCH, Ludhiana.

Co-Supervisor
Dr. Pavneet Kaur Selhi
Prof.,
Dept. of Pathology,
DMCH, Ludhiana.

Dr. Varun Gupta
Assoc. Prof.,
Dept. of Gastroenterology,
DMCH, Ludhiana.

The student has to submit the four copies of thesis (along with PDF format) , to the Controller of Examinations, BFUHS, Faridkot, at least six months before the commencement of theory examination, if he/she is otherwise eligible to take the examination. He /She must directed to attach a photocopy of this letter with the forwarding letter while submitting thesis to the University along with the letter of approval of University for change of supervisor/Co-Supervisor, change of topic,(if any).

SPSingh

Dr. S P Singh MS(Oph)
Controller of Examinations

Note :

1. *If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.*
2. *The student may submit the thesis as per the schedule already conveyed i.e for May/June examination 30th Nov of the preceding the year of examination and for Nov/Dec examinations 31st May of the year of examination.*

RED CELL DISTRIBUTION WIDTH AND RATIO OF RED CELL DISTRIBUTION WIDTH TO SERUM CALCIUM AS PREDICTORS OF OUTCOME OF ACUTE PANCREATITIS

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED

IN PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

MASTER OF SURGERY

In

GENERAL SURGERY

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES

FARIDKOT

DECEMBER, 2018

DR. SAVJOT SINGH NARANG

DEPARTMENT OF GENERAL SURGERY

DAYANAND MEDICAL COLLEGE AND HOSPITAL

LUDHIANA

ABSTRACT OF PLAN OF THESIS

Title	RED CELL DISTRIBUTION WIDTH AND RATIO OF RED CELL DISTRIBUTION WIDTH TO SERUM CALCIUM AS PREDICTORS OF OUTCOME OF ACUTE PANCREATITIS
For the degree of	M.S. GENERAL SURGERY
Name of the candidate	Dr Savjot Singh Narang
Supervisor	Dr Chiranjiv Singh Gill Professor, Department of Surgery
Co-supervisor	Dr Pavneet Kaur Selhi, Professor, Department of Pathology Dr Varun Gupta, Associate Professor, Department of Surgery
Institution	Dayanand Medical College & Hospital, Ludhiana
University	Baba Farid University of Health Sciences, Faridkot

Introduction: Acute pancreatitis is an acute inflammation of pancreas induced by activation of pancreatic enzymes by variety of causes of which gall stones and alcohol are the most common. Current severity scores include multiple variables, the results of which are available only after 48 hrs of admission. Red cell distribution width and serum calcium are simple routine parameters that seem to be related to inflammatory status and results of which are readily available.

Aims of Study: In acute pancreatitis, to evaluate red cell distribution width and ratio of red cell distribution width to serum calcium within 24hours of admission as predictors of outcome (severity and mortality) and in-hospital intervention (medical/percutaneous drainage/surgical) required by patient

Material & Methods: Values of red cell distribution width and serum calcium along with data regarding treatment given i.e medical or invasive(percutaneous drainage or necrosectomy) will be collected in this prospective randomized study of acute pancreatitis patients who will be admitted in DMCH, Ludhiana over a period of 1 year spanning from 1 Jan, 2019 to 31 Dec, 2019. Diagnosis and severity will be defined in accordance with the Revised Atlanta Classification 2012

Clinical Significance: As acute pancreatitis is associated with considerable mortality and morbidity, early detection and appropriate evaluation of severity will ensure early treatment and hence reduce mortality. So, it is important to identify a simple, easy and sensitive marker for predicting the mortality associated with acute pancreatitis.

Keywords: Acute pancreatitis, Red cell distribution width, serum calcium, severity, in-hospital intervention, mortality.

(Signature)	(Signature)	(Signature)	(Signature)	(Signature)
Candidate	Co-supervisor	Co-supervisor	Supervisor	Principal

CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis titled **"RED CELL DISTRIBUTION WIDTH AND RATIO OF RED CELL DISTRIBUTION WIDTH TO SERUM CALCIUM AS PREDICTORS OF OUTCOME OF ACUTE PANCREATITIS"** exist in the Department of General Surgery, DMC&H, Ludhiana and will be provided to the candidate. We will see that the data being included in the thesis is genuine and is collected by the candidate himself under our supervision and guidance.

Supervisor

Dr. Chiranjiv Singh Gill
Professor
Department of Surgery
DMCH, Ludhiana

Co-Supervisor(s)

Dr. Pavneet Kaur Selhi
Professor
Department of Pathology
DMCH, Ludhiana

Dr. Varun Gupta
Associate Professor
Department of Surgery
DMCH, Ludhiana

Dr. Jaspal Singh
Professor & Head
Department of Surgery
DMCH, Ludhiana

Place : Ludhiana

Date : 15/12/18

APPROVAL PROFORMA
BY
RESEARCH & ETHICAL COMMITTEE
DAYANAND MEDICAL COLLEGE & HOSPITAL, LUDHIANA

Name of candidate	Dr. Savjot Singh Narang
Department	General Surgery
Topic of Thesis	RED CELL DISTRIBUTION WIDTH AND RATIO OF RED CELL DISTRIBUTION WIDTH TO SERUM CALCIUM AS PREDICTORS OF OUTCOME OF ACUTE PANCREATITIS
Likely date of appearing in PG examination	May, 2021
Date of enrollment	10th May, 2018
Name of Head of Department	Dr. Jaspal Singh
1) Supervisor **2) Co-Supervisor(s)**	Dr. Chiranjiv Singh Gill Dr. Pavneet Kaur Selhi Dr. Varun Gupta
Signature of Members of Research Committee with Stamp	**Signature of Members of Ethics Committee with Stamp**
1. HOD Pharmacology	1. HOD Physiology
2. HOD Surgery	2. HOD Pathology
3. HOD Pathology	3. HOD Pharmacology
4. HOD Medicine	4. HOD SPM
5. Dean Academics	5. HOD Medicine
6. Vice Principal	6. HOD Surgery
	7. HOD Obst. & Gynae
	8. Legal Expert
	9. Secretary, IEC
	10. Dean Academics
	11. Vice Principal
	12. Principal

Approved: Yes / No

Chairperson
Research Committee

Chairperson
Research Committee

Approved: Yes / ~~No~~

Chairperson
Ethics Committee

Chairperson
Ethics Committee

BABA FARID UNIVERSITY OF HEALTH SCIENCES, FARIDKOT

PROFORMA FOR REGISTRATION OF SUBJECT FOR DISSERTATION

1	NAME OF THE CANDIDATE AND ADDRESS	Dr. Savjot Singh Narang House No 630/16/02 B-1, Kundanpuri, Civil Lines, Brindaban Road, Ludhiana
2	NAME OF THE INSTITUTE	Dayanand Medical College and Hospital, Ludhiana
3	COURSE OF STUDY AND SUBJECT	M.S. General Surgery
4	DATE OF ADMISSION OF COURSE	10-05-2018
5	TITLE OF THE TOPIC	RED CELL DISTRIBUTION WIDTH AND RATIO OF RED CELL DISTRIBUTION WIDTH TO SERUM CALCIUM AS PREDICTORS OF OUTCOME OF ACUTE PANCREATITIS

6. BRIEF RESUME OF THE INTENDED WORK

6.1 NEED FOR THE STUDY

Acute pancreatitis (AP) is an acute inflammation of the pancreatic parenchyma induced by activated pancreatic enzymes due to multiple causes.[1] Prognosis of AP depends on its severity, currently classified as mild, moderately severe and severe, according to the revised Atlanta classification (RAC) 2012, which emphasizes the presence of persistent organ failure using the Modified Marshall (MM) score.[2]

Although most patients have a mild disease, 20% of AP patients develop a severe clinical course associated with significant morbidity and mortality (7-42%).[1] Early identification of patients at increased risk of severe and fatal AP is crucial to improve prognosis through a prompt medical, endoscopic or percutaneous treatment and admission to a specialized intensive care unit. An ideal marker/prognostic score should be simple, economic, noninvasive, accurate, and quantitative.[3]

Several prognostic scoring systems and biological markers have been used to predict mortality in AP.[3] However, most of them are complex, require expensive investigations and not applicable early enough. Ranson and Bedside Index for Severity in AP (BISAP) are specific and widely used prognostic scoring systems due to easy evaluation and availability in the first 24 h.[3]

Single serum markers have also been evaluated and among them C-reactive protein (CRP) was found to be useful.[4] CRP ≥15 mg/dL at 48 h was found to be a predictor of poor prognosis. However, CRP has a predictive value only at 48h and hence it is a limited severity discriminator in the early phase of

AP.[3,5]

In previous studies, several AP scoring systems and laboratory tests have been proposed and developed to estimate the prognosis of AP, such as Ranson's score, Balthazar score, BISAP score and SIRS score, C-reactive protein (CRP), serum blood urea nitrogen (BUN), D-dimer and pro-calcitonin levels.[6] However, there are multiple disadvantages associated with these scoring systems like hassle of calculations and need for specific tests.[6] Until now, no single serum marker is able to predict mortality in AP at admission.

Red cell distribution width (RDW) measures the heterogeneity of size of red blood cell (RBC) in the peripheral blood, morphologically, known as anisocytosis. It is a routine parameter of the complete blood count test, described as simple, easy, inexpensive and quantitative test. RDW has been associated with inflammatory markers such as CRP, interleukin-6 and fibrinogen. It is commonly performed in the assessment of almost all the patients at the time of admission.[7] Conventionally, RDW has been used as a tool to explore the etiologies of anemia.[7] During the past decade, accumulated studies have shown that RDW is associated with the risk, disease activity and prognosis of various diseases, such as malignancies[8], heart failure[9], autoimmune diseases[10] and hepatocellular carcinoma[11] etc. It revealed to be a good predictor of mortality risk in elderly, critically-ill patients and patients with acute or chronic cardiovascular and respiratory diseases.[12] Besides those conditions, RDW has also been evaluated as a mortality predictor in AP.[13-15]

Hypocalcemia is a frequent finding in AP and has been associated with the severity of AP and thus serum calcium is routinely done in a patient

diagnosed with AP.

Severe AP is associated with many local complications which require surgical intervention. Complications of AP include acute fluid collection, sterile pancreatic necrosis, infected pancreatic necrosis, pancreatic abscess, pseudocyst, pancreatic ascites, portal/splenic vein thrombosis and pseudoaneurysm. These complications may require interventions like PCD drainage, necrosectomy, open drainage, closed drainage, angioembolisation of pseudoaneurysm or surgery, etc. Thus early detection of these complications is necessary to decide the appropriate intervention timely and thus decrease morbidity and mortality of patients diagnosed with AP

In our study we will use RDW and ratio of RDW to total serum calcium (TSC) values to predict outcome and in-hospital intervention required by patient of AP. This will decrease the burden of unnecessary expensive tests and scores which require complicated calculations. This will also allow to timely plan for interventions which in return would help to decrease morbidity and mortality of the patients.

6.2 REVIEW OF LITERATURE

Marta Gravito-Soares et al [16] conducted a retrospective study in 2018 on patients admitted with AP between 2014-2016 to find out RDW and RDW to TSC ratio as major predictors of severity and mortality in AP. This study concluded the good predictive power of RDW, evaluated at admission and in the first 24 h, as well as RDW-to-TSC ratio for both severity and mortality in AP, being superior to Ranson, BISAP and MM scores. RDW > 13.0 and RDW-to-TSC > 1.4 were excellent predictors for AP severity. RDW> 14.0 and RDW-to-TSC > 1.7 were accurate predictors for AP mortality.

Hemant Goyal et al [14] conducted a systemic review on prognostic value of admission RDW in AP. The study found out the predictive value of some well-recognized score systems in AP, including acute physiology and chronic health evaluation (APACHE) score, BISAP, Ranson score, Glasgow score were comparable to RDW. RDW is a strong prognostic factor for AP. RDW is independently associated with mortality in AP. This study indicated that RDW has utility in estimating the prognosis of AP.

Tao Peng et al [17] conducted a retrospective study in 2017 on assessment of RDW as an early predictor of persistent organ failure in patients with AP. The study results suggested that RDW was an independent prognostic factor of persistent organ failure in AP. The RDW is a convenient and cheap laboratory test that could be routinely utilized in clinical setting.

Cetinkaya E et al [18] conducted a retrospective study in 2014 to evaluate the accuracy of RDW to platelet ratio (RPR) to predict in-hospital mortality of patients diagnosed with AP. The study concluded that RPR obtained on hospital admission was persistently higher among non-survivors than among

survivors (P < 0.0001). The median RPR was 0.000087 in the non-survivor group and 0.000058 in the survivor group. RPR with a cutoff value of 0.000067 presented an area under the curve of 0.783 (95% CI: 0.688-0.878) in receiver operating characteristic curves and could predict the mortality of approximately 80% of the patients.

Kazim senol et al [12] conducted a study on RDW as a predictor of mortality in AP. The study concluded that RDW has a very good discriminative power for mortality. With a cutoff value of 14.8 for RDW, mortality could be correctly predicted in approximately 77% of cases.

Robert M. O'Connell et al [19] conducted a retrospective cohort study on patients admitted with AP between august 2013-2016 on RDW and neutrophil to lymphocyte ratio (NLR) as predictors of outcome in AP. The study found out that RDW above the upper limit of normal (ULN) was associated with a significantly increased likelihood of admission to ICU or HDU and patients who had a NLR above 5 on presentation were also at increased risk of ICU or HDU admission. Patients who had both a RDW above the ULN and a raised NLR had an increased risk of inpatient mortality.

Ting Zang et al [20] conducted a mixed retrospective and prospective study to predict the severity of AP based on RDW at an early stage in patients admitted in Shanghai Tenth People's Hospital. The study found a higher RDW in patients with moderately severe and severe AP. RDW values were also found positively correlated with the patient's blood urea nitrogen, creatinine, age, and bedside index of severity in acute pancreatitis scoring system, and were negatively correlated with the serum albumin. The optimal cutoff value for RDW to predict whether patients with AP should be in intensive care unit

(ICU) was 13.55 with a sensitivity of 54.5% and a specificity of 73.6%. In the validation study, AP with RDW ≥ 13.55% had significantly higher ICU admission ratio than those with RDW<13.55%. In conclusion, RDW is positively associated with AP severity, and is likely a useful predictive parameter of AP severity.

Yao J et al [21] conducted a cross sectional study to find association between RDW and AP. The study found out higher RDW values among non-survivors of patients with AP. Patients with AP with the highest RDW values had the lowest levels of Ca, total protein, albumin, haemoglobin, white and red blood cell count, but the highest mortality. With a cut-off value of 14.2 for RDW, sensitivity and specificity of RDW to predict mortality were 75.0% and 89.8%, and Kaplan-Meier analysis showed an increase in probability of death with high RDW values.

Dong Wang et al [13] conducted a retrospective cohort study to investigate the association between the RDW and mortality in patients with AP. The study found out RDW as a good prognostic predictor of death in AP patients. Increased RDW can be used as a new indicator of mortality in patients with AP. In addition, a cut-off RDW value of 14.35 with a sensitivity of 88.2% and a specificity of 91.8 was identified.

A.A.Gutiérrez-Jiménez et al [22] conducted a study to evaluate TSC and albumin-corrected calcium (ACC) as prognostic severity factors in AP. The study concluded TSC and ACC, measured within the first 24 hours, are useful severity predictors in AP, with sensitivity and predictive values comparable or superior to those of the conventional prognostic scales. The maximum TSC cut-off point was 7.5 mg/dL, with values of S, 67%; Sp, 82%; PPV, 27%, and

NPV, 96%. The maximum ACC cut-off point was 7.5 mg/dL, with values of S, 67%; Sp, 90%; PPV, 40%; NPV, 96%. Both had values similar to those of the Ranson and APACHE II prognostic scales.

6.3 AIMS AND OBJECTIVES OF THE STUDY

In AP, to evaluate red cell distribution width and ratio of red cell distribution width to serum calcium within 24hours of admission as predictors of

- outcome (severity and mortality)
- in-hospital intervention (medical/percutaneous drainage/surgical) required

7. MATERIALS AND METHODS

7.1 Source of Data

Patients who will be admitted to Dayanand Medical College and Hospital, Ludhiana with AP from 1st January, 2019 to 31st December, 2019

7.2 METHOD OF COLLECTION OF DATA

Variables evaluated included age, gender, co-morbidities, smoking habits, alcohol consumption, AP etiology, organ failure and local/systemic complications AP-associated. Biochemical tests will include routine investigations done in a patient with AP such as serum calcium levels along with hematological tests like RDW as a part of complete blood count in first 24 hours of admission. In addition, data of treatment provided i.e medical or invasive (PCD or necrosectomy), intensive care unit stay and patients who will expire as a result of AP will also be collected.

INCLUSION CRITERIA

- Age over 18 years
- Minimum hospital stay of 24 h,
- Cases presenting within 5 days of onset of symptoms
- A diagnosis of AP according to the RAC (at least two criteria: typical clinical presentation including acute persistent abdominal pain, serum amylase exceeding 3 times the upper limit of normal (100 IU/L) and characteristic findings on abdominal ultrasonography and/or computed tomography).
- AP severity will also be defined according to the RAC, based on the presence of single or multiple persistent organ failure (> 48 h) and/or local complications.

- Organ failure will be classified according to MM including cardiovascular, respiratory and renal failures.

EXCLUSION CRITERIA

- Factors affecting RDW, such as infectious or immunosuppressive conditions/therapy, active malignancy, chronic use of erythropoietin, recent transfusion history, pregnancy or trauma.
- Factors affecting TSC, such as parathyroid disorders, malignancies, use of thiazides or granulomatous disorders like sarcoidosis

DURATION OF STUDY

This study will be conducted at DMCH, Ludhiana from 1st January, 2019 to 31st December, 2019.

OUTCOME

This study will evaluate role of RDW and ratio of RDW to TSC as predictors of outcome and in-hospital intervention required in patients diagnosed with AP

STATISTICAL ANALYSIS

Data will be described in terms of range; mean ± standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. Comparison of quantitative variables between the study groups will be done using Student t-test and Mann Whitney U test for independent samples for parametric and non-parametric data respectively. For comparing categorical data, Chi square ($\chi 2$) test will be performed and exact test will be used when the expected frequency is less than 5. Sensitivity, specificity, positive and negative predictive values and accuracy of each method and its confidence interval (95% CI) will be also determined, besides the Youden index (probability of correct classification) and determining the

area under the ROC curve. A probability value (p value) less than 0.05 will be considered statistically significant. All statistical calculations will be done using SPSS (Statistical Package for the Social Science) SPSS 21 version statistical program for Microsoft Windows.

7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.

The study does not require any investigation or intervention other than those routinely done for every patient for acute pancreatitis

7.4 HAS ETHICAL CLEARANCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3?

Attached along with

LIST OF REFERENCES

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PROFORMA

SR. NO.: **MRD NO.:**

NAME: **AGE:** **SEX:**

ADDRESS:

DATE OF ADMISSION: **DATE OF DISCHARGE:**

HOSPITAL STAY:

ICU/HDU STAY:

CHIEF COMPLAINTS:

HISTORY OF PRESENT ILLNESS:

PAST HISTORY

MALIGNANCY:

CHRONIC STEROID USE:

DIABETES:

HYPERTENSION:

GRANULOMATOUS DISORDERS:

COPD:

CARDIOVASCULAR:

DRUGS USE:

TRANSFUSION HISTORY:

OTHERS:

Signature of Candidate **Signature of Supervisor**

PERSONAL HISTORY

ALCOHOL ABUSE:

SMOKING:

OTHERS:

GENERAL EXAMINATION:

VITALS(ON ADMISSION)

HR BP RR TEMP

Built Nutrition

GCS Pallor Edema Icterus

Cyanosis Lymphadenopathy Clubbing

JVP

SYSTEMIC EXAMINATION

ABDOMEN:

INSPECTION

PALPATION

PERCUSSION

AUSCULTATION

RESPIRATORY

CVS

CNS

ETIOLOGY OF AP

Signature of Candidate **Signature of Supervisor**

INVESTIGATIONS (ON ADMISSION):

HB: RDW:

TLC: PLATELET COUNT:

RANDOM BLOOD SUGAR:

BLOOD UREA: SERUM CREATININE:

SERUM AMYLASE: SERUM LIPASE:

SERUM CALCIUM: RDW:TSC-

CHEST X-RAY:

USG ABDOMEN:

CT ABDOMEN(IF AVAILABLE):

PaO2: FiO2:

PaO2/FiO2:

COMPLICATIONS:

Signature of Candidate Signature of Supervisor

MANAGEMENT- MEDICAL OR INVASIVE(PCD OR SURGICAL)

OUTCOME:

Signature of Candidate

Signature of Supervisor

INFORMED PATIENT CONSENT

Date: _____

I.....D/o, W/o,

S/o..... .....am willing to participate in the study **"RED CELL DISTRIBUTION WIDTH AND RATIO OF RED CELL DISTRIBUTION WIDTH TO SERUM CALCIUM AS PREDICTORS OF OUTCOME OF ACUTE PANCREATITIS"** The procedure with its complications has been explained to me in local vernacular language. I have fully understood that no special tests and extra expenditure in any form, merely for the purpose of thesis is being carried out. I am free to opt out the study any time without assigning any reason.

....

Signature of the Witness Signature of the patient

Name:

Signature of Candidate **Signature of Supervisor**

मरीज अनुमति फार्म

तिथि _____

मैं _____ पत्नी/पुत्र/पुत्री _____ निवासी _____ इस शोधकार्य "**RED CELL DISTRIBUTION WIDTH AND RATIO OF RED CELL DISTRIBUTION WIDTH TO SERUM CALCIUM AS PREDICTORS OF OUTCOME OF ACUTE PANCREATITIS**" में भाग लेने के लिए सहमत हूँ। मैं इस शोधकार्य में भाग लेने के लिए अपनी स्वेच्छा से तैयार हूँ। मैं पुष्टि करता/करती हूँ की यह स्वीकृति देने के लिए मुझे कोई आर्थिक प्रलोभन नहीं दिया गया और न ही दबाव डाला गया है। मुझे इस शोधकार्य का उद्देश्य स्पष्ट कर दिया गया है और मुझे यह विश्वास है की यह विज्ञान और मानवता के लाभ के लिए है। मुझे इस शोधकार्य में होने वाले जोखिम के बारे में समझा दिया गया है और मेरी समझ में यह जोखिम बहुत मामुली है।

मैं इस शोधकार्य में भाग लेने के सम्बन्ध में किसी भी समय अपनी अस्वीकृति व्यक्त कर सकता/सकती हूँ और मेरे अस्वीकृति व्यक्त करने का मेरे इलाज पर कोई प्रभाव नहीं पड़ेगा।

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गवाह के हस्ताक्षर
नाम:

_____
रोगी के हस्ताक्षर/अंगूठे का निशान
नाम:

_____
अन्वेषक के हस्ताक्षर

_____
विद्यार्थी के हस्ताक्षर

ਮਰੀਜ਼ ਰਜ਼ਾਮੰਦੀ ਫਾਰਮ

ਮਿਤੀ_____

ਮੈ_____ਪਤਨੀ/ਪੁੱਤਰ/ਪੁੱਤਰੀ_____

ਵਾਸੀ _____

"RED CELL DISTRIBUTION WIDTH AND RATIO OF RED CELL DISTRIBUTION WIDTH TO SERUM CALCIUM AS PREDICTORS OF OUTCOME OF ACUTE PANCREATITIS" ਤੇ ਚਲ ਰਹੀ ਖੋਜ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਰਜ਼ਾਮੰਦ ਹਾਂ। ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਮੈ ਆਪਣੀ ਮਰਜ਼ੀ ਨਾਲ ਤਿਆਰ ਹਾਂ। ਮੈ ਇਹ ਦਸਣਾ ਚਾਹੁੰਦਾ ਹਾਂ/ ਚਾਹੁੰਦੀ ਹਾਂ ਕੇ ਇਹ ਰਜ਼ਾਮੰਦੀ ਦੇਣ ਵਾਸਤੇ ਮੈਨੂ ਕਿਸੇ ਵੀ ਤਰਾਂ ਦਾ ਲੋਭ-ਲਾਲਚ ਨਹੀ ਦਿੱਤਾ ਗਿਆ ਅਤੇ ਨਾ ਹੀ ਕੋਈ ਦਬਾ ਪਾਇਆ ਗਿਆ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਦਾ ਮਨੋਰਥ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਭਰੋਸਾ ਦਵਾਇਆ ਗਿਆ ਹੈ ਕੇ ਇਹ ਖੋਜ ਵਿਗਿਆਨ ਅਤੇ ਮਾਨਵਤਾ ਦੀ ਭਲਾਈ ਲਈ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਵਿਚ ਹੋਣ ਵਾਲੇ ਖਤਰੇ ਬਾਰੇ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਯਕੀਨ ਹੈ ਕੇ ਇਹ ਖਤਰਾ ਬਹੁਤ ਮਾਮੂਲੀ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਦਾ ਢੰਗ – ਤਰੀਕਾ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ।

ਮੈ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਬਾਰੇ ਆਪਣੀ ਰਜ਼ਾਮੰਦੀ ਕਿਸੇ ਵੀ ਸਮੇ ਵਾਪਸ ਲੈ ਸਕਦਾ ਹਾਂ/ ਸਕਦੀ ਹਾਂ ਅਤੇ ਮੇਰੀ ਰਜ਼ਾਮੰਦੀ ਵਾਪਸ ਲੈਣ ਦਾ ਮੇਰੇ ਇਲਾਜ ਤੇ ਕੋਈ ਅਸਰ ਨਹੀ ਹੋਵੇਗਾ।

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ਗਵਾਹ ਦੇ ਹਸਤਾਖਰ ਮਰੀਜ਼ ਦੇ ਹਸਤਾਖਰ

ਮਿਤੀ_____ ਮਿਤੀ_____

ਪਤਾ _____ ਪਤਾ _____

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ਨਿਰੀਖਕ ਦੇ ਹਸਤਾਖਰ

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ਸਿਖਿਆਰਥੀ ਦੇ ਹਸਤਾਖਰ